### Journal of Clinical Periodontology

# The relationship between tomato intake and congestive heart failure risk in periodontitis subjects

Wood N, Johnson RB: The relationship between tomato intake and congestive heart failure risk in periodontitis subjects. J Clin Periodontol 2004; 31: 574–580. doi: 10.1111/j.1600-051X.2004.00531.x. © Blackwell Munksgaard, 2004.

#### Abstract

**Background:** The objective of this study was to investigate the relationship between monthly tomato consumption (MTC) and serum lycopene (sLyco) levels, and a selfreported history of congestive heart failure (CHF) in individuals with periodontitis using data available in the Third National Health and Nutrition Examination Survey (NHANES III).

**Methods:** Adult participants in NHANES III were used in this study. Zero to thirty three percent of sites with a periodontal attachment loss (PAL) of >3 mm was considered a healthy periodontium, while greater than >33% of sites with PAL of >3 mm as periodontitis. The outcome variable was the self-reported history of CHF. MTC and sLyco levels were categorized into quartiles. Data was analyzed by Kruskal–Wallis, ANOVA and multivariate analyses using SPSS<sup>®</sup>. p < 0.05 was used to reject the null hypothesis.

**Results:** Individuals with periodontitis showed a dose–response relationship between dietary MTC and self-reported CHF risk; moderate MTC (risk ratio (RR), 3.15; 95% confidence interval (CI), 1.03–9.67), low MTC (RR, 3.31; 95% CI, 1.33–8.24)

(p < 0.05) and very low MTC (RR, 5.10; 95% CI, 1.67–15.57) (p < 0.01), adjusting for confounders of both diseases (periodontitis and CHF). The moderate sLyco level-healthy periodontium group showed a significant decrease in CHF risk (RR, 0.25; 95% CI, 0.07–0.84) (p < 0.05), adjusting for confounders. Significant inverse dose–response relationships were seen between sLyco and C-reactive protein, and MTC and white blood cell count in periodontitis subjects, respectively (p < 0.05). MTC was correlated with sLyco concentration (r = -0.018, p < 0.05), adjusting for confounders abolished that significance.

**Conclusions:** A relationship exists between periodontitis and CHF risk, and high MTC appears to affect this relationship in a positive direction in periodontitis subjects.

#### Nelson Wood and Roger B. Johnson

Department of Periodontics, University of Mississippi School of Dentistry, Jackson, MS, USA

Key words: carotenoids; congestive heart failure; periodontitis; serum lycopene; tomatoes

Accepted for publication 9 September 2003

Congestive heart failure (CHF) is a major cause of death in the United States, affecting 4.8 million Americans (NHLBI 1996). It is a complex clinical syndrome characterized by exertional dyspnea, fatigue and often peripheral edema resulting from left ventricular dysfunction. Specific mechanisms underlying these symptoms remain poorly understood; however, CHF always occurs as a consequence of other cardiac diseases, with coronary artery disease being the most common etiologic factor for left ventricular systolic dysfunction. Preventing plaque from developing in coronary arteries could have profound effects on the incidence of CHF, in addition to dietary lipid reduction, blood pressure control, smoking cessation, weight reduction and exercise (Forrester et al. 1996, NHLBI 1996).

Lycopene, a carotenoid without provitamin-A activity, is one of the major carotenoids in Western diets, and is found primarily in tomatoes and tomato products. It accounts for about 50% of carotenoids in human serum. In contrast to other carotenoids, serum lycopene (sLyco) levels are not usually reduced by smoking or alcohol consumption but are reduced by increased age. Also, reduced sLyco concentration has been reported in patients with inflammatory diseases (Gerster 1997). Epidemiological studies suggest a cardioprotective role for carotenoid-rich foods (Chopra et al. 2000), with numerous observational studies showing that individuals who ingest more dietary carotenoids have a reduced risk of several chronic diseases, including cardiovascular diseases (Mayne 1996). Among the carotenoids, lycopene is commonly present within the serum and other tissues. Serum and tissue lycopene levels were inversely related to chronic disease risk (Rao & Agarwal 2000), and exhibited a protective function in the development of atherosclerosis (Klipstein-Grobusch et al. 2000) and myocardial infarction (Kohlmeier et al. 1997).

Recent reports suggest that periodontitis may be a risk factor for cardiovascular diseases (Beck et al. 1998, Arbes et al. 1999, Loos et al. 2000). In addition, acknowledged risk factors for cardiovascular diseases are also risk factors for periodontal disease (Grossi & Genco 1998). Periodontitis is a chronic inflammation of the supporting tissues of the teeth and affects 75% of the adults in the United States (Genco et al. 2002). Bacteria within dental plaque are a major factor for the initiation and progression of this disease. There is general agreement that various systemic diseases may be risk factors in the etiology of periodontal disease. Increasing evidence exists for a bi-directional relationship between the etiologies of both systemic and periodontal diseases (Wu et al. 2000, Fowler et al. 2001, Taylor 2001). A causal association between systemic diseases and periodontitis has not been established; however, systemic factors likely modify the host response to bacteria and bacterial lipopolysaccharides (LPS), resulting in specific forms and patterns of periodontal diseases (Kinane & Marshall 2001). Periopathogenic bacterial LPS, initiate a cascade of proinflammatory cytokines, having both local and systemic effects, including activation of monocytes/macrophages, increased neutrophil numbers and plasma fibrinogen concentrations along with other coagulation factors. Alterations in lipid metabolism, and enhancement of the synthesis of acute phase proteins such as Creactive protein (CRP) and interleukin-6 (IL-6) also occur in patients with

periodontal disease (Loos et al. 2000, Slade et al. 2000, Wu et al. 2000). There are several reports suggesting that several periopathogenic bacteria are present within atheromatous plaque and have direct effects on blood platelet activation and aggregation, suggesting that they may be factors in the initiation and progression of atherosclerosis (Herzberg et al. 1983, Herzberg & Meyer 1996, Haraszthy et al. 2000).

There is not extensive data concerning the relationship between sLyco concentrations and the incidence of periodontal disease. The purpose of this study is to determine whether relationships exist between sLyco concentrations, periodontal disease, and CHF and whether a relationship exists between low sLyco and CHF risk in periodontal subjects. Since lycopene is derived from tomatoes, we also included tomato consumption, in order to study the relationship between dietary intake of tomatoes, sLyco concentrations, and the incidence of periodontal disease and CHF risk using the Third National Health and Nutrition Examination Survey (NHANES III) data.

#### Materials and Methods

Data for this study was obtained from NHANES III, conducted from 1988 to 1994, designed to provide estimates of the health status of the United States' civilian, non-institutionalized population aged 2 months and over (Ezzati et al. 1992). For this analysis, three public use data files - household adult (USDHHS 1996a), examination (USDHHS 1996b) and laboratory (USDHHS 1996c) - were obtained from CD-ROM and merged into one data file. Subjects, aged 18 years and greater, were used in this study. The independent variable of interest was the percent of sites per subject with a periodontal attachment loss (PAL) of >3 mm. Periodontal examinations were conducted in the mobile examination centers by six calibrated examiners (Arbes et al. 1999). For this study, extent scores (Carlos et al. 1986), representing the percent of sites per subject with attachment loss of 3 mm or greater, were calculated and categorized into two groups.

Zero to thirty-three percent of sites with PAL of >3 mm was considered normal, while greater than >33% of sites with PAL>3 mm was defined as periodontitis. The threshold of 3 mm was used to increase the likelihood that attachment loss was the result of disease and not measurement error. This grouping was consistent with other studies reporting NHANES III data (Arbes et al. 1999). The analysis excluded persons who were edentulous.

Another outcome variable was the self-reported history of CHF. The administration of food-frequency questionnaires and a detailed 24 h dietary recall was used to record food consumption. Monthly tomato consumption (MTC) was calculated and divided into quartiles: 0-3 tomatoes were considered very low; >3-9 was low; >9-17 was moderate; and >17 was high consumption.

Non-fasting, venous blood was collected and analyzed for CRP level and white blood cell (WBC) count (USDHHS 1996c). sLyco ( $\mu g$ /dl) was also analyzed, calculated and categorized into quartiles: 0–14 was considered very low; >14–21 was low; >21–29 was moderate; and >29 was a high concentration.

Data was analyzed using SPSS version 10.1. Group comparisons were made using Kruskal-Wallis, ANOVA, multivariate general linear models using a Bonferroni adjustment, and multivariate logistic regression to calculate crude odds ratios. Established risk factors for periodontal disease and CHF were selected covariables. The covariables were age, race, gender, body mass index (BMI), smoking history, a self-reported history of diabetes (self-reported by "Has the doctor ever told you that you have diabetes?"), hypertension, socio-economic status [poverty income ratio (unimputed income)], education level (years), serum CRP and WBC. Furthermore, in order to determine if this effect was due to exogenous lycopene, or lycopene derived from tomato consumption, we controlled for lycopene in the tomato multinominal logistic regression model as well as other serum antioxidants (serum carotene, serum vitamin E and serum vitamin C). While, in the lycopene multinominal logistic regression model, we controlled for tomato intake and the other above-mentioned serum antioxidants, p < 0.05 was used to reject the null hypothesis.

#### Results

#### **Baseline findings**

Subjects with periodontitis had risk factors including demographics, smok-

#### 576 Wood & Johnson

Table 1. Baseline demographics, medical conditions, mean blood chemistry and mean antioxidants

Baseline characteristics	No periodontology $(n = 1443)$	Yes periodontology $(n = 4087)$	No CHF ( <i>n</i> = 17054)	Yes CHF $(n = 640)$
demographics	mean (SEM)		mean (SEM)	
age (years)	47.7 (0.6)	47.7 (0.4)	46.7 (0.1)	$68.8 (0.5)^*$
male (%)	52.4	48.6	48.9	46.6
Race (%)				
Caucasian 27.2		72.8	95.3	4.7
African-American	27.0	73.0	96.3	3.7
other	23.4	76.6	97.5	2.5
education level (years)	10.76 (0.12)	10.76 (0.07)	10.79 (0.03)	10.72 (0.14)
poverty index	231.9 (5.6)	239.9 (3.6)	240.1 (1.4)	186.1 (6.0)*
CHF risk factors				
systolic BP (mmHg)	111.03 (0.28)	116.07 (0.21)*	118.38 (0.18)	117.30 (0.90)
diastolic BP (mmHg) 65.90 (0.29)		70.82 (0.17)*	68.71 (0.12)	67.92 (0.64)
pulse rate (beats/min) 73.46 (0.29)		73.77 (0.18)	75.61 (0.11)	75.24 (0.49)
diabetes history (% yes) 7.9		8.1	7.3	28.4*
body mass index 23.58 (0.17)		23.91 (0.10)	23.54 (0.05)	23.69 (0.25)
waist to hip ratio	0.909 (.002)	0.909 (.001)	0.908 (0.001)	0.909 (0.003)
smoking (packs/day)	1.11 (0.18)	1.23 (0.16)	1.19 (0.05)	1.56 (0.46)
current smoker (% yes)	53.6	50.5	52.0	28.1
Blood chemistry				
serum CRP (mg/dl) 0.45 (0.02)		0.46 (0.02)	0.42 (0.01)	0.43 (0.03)
WBC count $(\times 10^9/l)$ 7.27 (0.06)		7.42 (0.04)	7.37 (0.02)	7.41 (0.09)
Antioxidants				
serum carotene ( $\mu$ g/dl)	478.4 (24.1)	457.4 (13.5)	434.9 (6.1)	422.1 (34.4)
serum tocopherol (µg/dl)	8.52 (0.22)	8.55 (0.15)	8.29 (0.07)	7.84 (0.33)*
serum vitamin C (mg/dl)	0.786 (0.014)	0.769 (0.008)	0.751 (0.004)	0.773 (0.019)

\**p*<0.05.

ing, medical conditions, inflammatory biomarkers and antioxidant intake. When compared with healthy subjects, periodontitis subjects had significantly higher systolic and diastolic blood pressures (p < 0.05), and had higher BMI and lower serum vitamin C. Individuals with a history of CHF also had risk factors including demographics, smoking, medical conditions, inflammatory markers and antioxidant intake. When compared with individuals reporting no history of CHF, individuals with a history of CHF were significantly older, poorer and reported a history of diabetes (p < 0.05). CHF subjects also had higher BMI and lower serum carotene and tocopherol levels (Table 1).

## Periodontitis and inflammatory biomarkers

Various dose–response relationships between sLyco levels in individuals with periodontitis and healthy periodontium were explored using a Bonferroni adjustment of the data (Table 2). When the analyses were restricted to individuals with periodontitis, a significant relationship was found between serum CRP levels and periodontitis (p < 0.05), When analyses were restricted to individuals with healthy periodontium, a strong trend was found for serum CRP *Table 2.* Relationships between lycopene quartiles, serum C-reactive protein (CRP) and white blood cell (WBC) count (mean  $\pm$  SEM) using a multivariate general linear model

Lycopene quartiles	Biomarker	No periodontology	Yes periodontology
very low low moderate	Serum CRP	$\begin{array}{c} 0.561 \pm 0.091 \\ 0.422 \pm 0.082 \\ 0.365 \pm 0.070 \end{array}$	$\begin{array}{c} 0.582 \pm 0.058^{NS} \\ 0.392 \pm 0.052^{*,NS} \\ 0.339 \pm 0.039^{*,NS} \end{array}$
high very low low moderate high	WBC count	$\begin{array}{c} 0.223 \pm 0.103 \\ 7.14 \pm 0.25 \\ 7.78 \pm 0.29 \\ 7.03 \pm 0.33 \\ 6.90 \pm 0.27 \end{array}$	$\begin{array}{c} 0.453 \pm 0.064^{*,NS} \\ 7.34 \pm 0.16^{NS} \\ 7.24 \pm 0.18^{NS} \\ 7.42 \pm 0.18^{NS} \\ 7.34 \pm 0.17^{NS} \end{array}$

Multivariate general linear model with a Bonferroni adjustment for gender, race, age, body mass index, smoking status, diabetes history, hypertension, socioeconomic status, education level, serum carotene, vitamin E, vitamin C and tomato consumption.

\*p < 0.05. There is only a significant relationship between yes periodontology, serum lycopene quartiles and CRP.

NS, there are no significant differences between the yes and no periodontology subjects for CRP or WBC at any serum lycopene quartiles.

and sLyco levels (p = 0.05). When analyses were stratified for sLyco quartiles in individuals with periodontitis versus individuals with healthy periodontium, no significant differences were seen in either CRP or WBC count and sLyco levels (Table 2).

Various dose–response relationships of different MTC in individuals with periodontitis and healthy periodontium were explored using a Bonferroni adjustment of the data (Table 3). When the analyses were restricted to individuals with periodontitis, a significant relationship was found in WBC count and periodontitis (p < 0.05). When analyses were stratified for MTC quartiles in individuals with periodontitis versus individuals with healthy periodontium, no significant differences were seen in either CRP or WBC count and MTC levels (Table 3).

#### Periodontitis and self-reported CHF risk

Multivariate logistic regression for individuals with periodontitis and individuals with healthy periodontium, stratified for MTC quartiles are shown in Table 4. Various dose–response

*Table 3*. Relationship between monthly tomato consumption (MTC) quartiles and serum C-reactive protein (CRP) and white blood cell (WBC) count (mean  $\pm$  SEM) using a multivariate general linear model

MTC quartiles	Biomarker	No periodontology	Yes periodontology
very low	serum CRP	$0.386\pm0.084$	$0.455 \pm 0.052^{\rm NS}$
low		$0.376 \pm 0.092$	$0.488 \pm 0.057^{ m NS}$
moderate		$0.397 \pm 0.051$	$0.370 \pm 0.034^{ m NS}$
high		$0.394 \pm 0.107$	$0.443 \pm 0.058^{ m NS}$
very low	WBC count	$7.36 \pm 0.26$	$7.58\pm0.16^{\rm NS}$
low		$7.20 \pm 0.25$	$6.97 \pm 0.15^{*,\mathrm{NS}}$
moderate		$7.22\pm0.30$	$7.36\pm0.20^{\rm NS}$
high		$7.38\pm0.35$	$7.43\pm0.19^{\rm NS}$

Multivariate general linear model with a Bonferroni adjustment for gender, race, age, body mass index, smoking status, diabetes history, hypertension, socioeconomic status, education level, serum carotene, vitamin E, vitamin C and tomato consumption.

p < 0.05. There is only a significant relationship between yes periodontology, MTC quartiles and WBC.

NS, there are no significant differences between the 'Yes' and 'No' periodontology subjects for CRP or WBC at any MTC quantities.

relationships were explored. Individuals with periodontitis showed a doseresponse relationship between dietary MTC and self-reported CHF risk; moderate MTC, low MTC and very low MTC (p < 0.05), adjusting for demographic, medical and lifestyle factors. Further adjusting for additional confounders for both periodontitis and CHF, inflammatory biomarkers (CRP and WBC count), the dose-response relationship increased between dietary MTC and CHF risk; moderate MTC, low MTC (p < 0.05) and very low MTC (p < 0.01). Further adjusting for serum carotenes, vitamin E and vitamin C increased the significance of the relationship between dietary MTC and CHF; moderate MTC, low MTC (p <0.05) and very low MTC (p < 0.01). When data were further adjusted for sLyco, the relationship between MTC and CHF risk in periodontally involved individuals remained high; moderate MTC, low MTC (p < 0.05) and very low MTC (p < 0.01).

No dose-response relationship was found between the sLyco levels and self-reported CHF risk in individuals with periodontitis (Table 5). However, the moderate sLyco level-healthy periodontium group showed a significant decrease in CHF risk (p < 0.05) adjusting for age, race, gender, BMI, smoking status, history of diabetes, hypertension, education level and socioeconomic status. Further adjustment for additional confounders for both periodontitis and CHF, inflammatory biomarkers (serum CRP and WBC count), showed a similar CHF risk reduction; moderate sLyco (p < 0.05). Further adjustment for serum

carotenes, vitamin E and vitamin C further reduced the relationship between sLyco and CHF risk even more; moderate MTC (p < 0.05). When we further adjusted for dietary MTC, the relationship between sLyco and CHF risk remained the same; moderate sLyco (p < 0.05).

#### Discussion

The results of this study provide evidence of a relationship between periodontitis subjects with very low MTC and a significantly elevated risk of CHF when compared with high MTC periodontitis subjects. MTC levels in individuals with healthy periodontium were not significantly associated with the risk of CHF (all were low). Inflammatory markers, CRP and WBC count, were not significantly associated with an elevated risk for CHF. The findings of this study did show evidence of significant inverse dose-response relationships between sLyco levels and CRP, and MTC and WBC, in the periodontitis subjects; and also demonstrated a decreased risk of CHF with moderate sLyco levels in individuals with a healthy periodontium. A positive relationship was found between high MTC and CHF risk in periodontally involved subjects.

Cross-sectional and prospective studies have established that elevated peripheral blood levels of several systemic inflammatory markers (including CRP) are associated with the risk of cardiovascular diseases and the severity of atherosclerosis (Berk et al. 1990, Maseri et al. 1996, Mendall et al. 1996, Ridker et al. 1999, 2000a, b, Liuizzo & Rizello 2001). In addition, high leukocyte counts are positively correlated with cardiovascular diseases (Kannel et al. 1992, Phillips et al. 1992).

In the present study, we observed a significant association between periodontitis and serum CRP, similar to those reported in other studies (Loos et al. 2000). We also observed significant associations between CRP and sLyco levels, and MTC and WBC in individuals with periodontitis (p < 0.05).

In our statistical analyses, we controlled for CRP and WBC count, which were associated with MTC levels in individuals with periodontitis (p < 0.05). Finally, we adjusted for tomato intake in the sLyco–CHF risk model and sLyco in the MTC–CHF risk model, to show that these results were due to tomato consumption levels, rather than sLyco, which were not significantly correlated after adjustments for confounders, except in the moderate sLyco-healthy periodontium subjects.

Lycopene, best known as an antioxidant, is mainly supplied by tomatoes, which contain many other beneficial substances (high levels of vitamin A, vitamin C, vitamin E, folate, potassium, bioflavonoids (especially quercetin) and phytosterols). Lycopene can be absorbed more efficiently by the body after it has been processed into juice, sauce, paste, or ketchup (Fuhrman et al. 1997). Tomato intake, in the form of juice, tomato oleoresin, tomato paste, tomato sauce and/or orange and red tomatoes, delayed and reduced low density lipoprotein (LDL) oxidation (Fuhrman et al. 2000, Upritchard et al. 2000).

In recent epidemiological studies, tissue and sLyco levels were inversely related to risk of coronary heart disease. Increases in LDL oxidation have been hypothesized to be causally associated with increasing risk of atherosclerosis and coronary heart disease (Agarwal & Rao 1998) and studies have shown contradictory lycopene effects on LDL oxidation (Carroll et al. 2000, Upritchard et al. 2000). As an antioxidant, lycopene has a singlet-oxygen-quenching ability twice as high as that of  $\beta$ carotene (a vitamin A relative) and 10 times higher than that of  $\alpha$ -tocopherol (a vitamin E relative) (Gerster 1997).

In this study, the differences between sLyco levels and MTC groups seen periodontitis subjects and CHF risk, may be reflective of tomatoes contain-

Periodontology status	MTC	RR for CHF Y versus N (95% CI)*	RR for CHF Y versus N (95% CI) <sup>†</sup>	RR for CHF Y versus N (95% CI) <sup>‡</sup>	RR for CHF Y versus N (95% CI) <sup>§</sup>
Y	high	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	moderate	2.14 (0.83,5.55)	3.15 (1.03,9.67)	2.66 (0.85,8.31)	2.70 (0.86,8.44)
	low	2.03 (0.93,4.43)	3.31 (1.33,8.24)**	3.42 (1.28,9.13)**	3.35 (1.26,8.93)**
	very low	3.35 (1.30,8.64)**	5.10 (1.67,15.57)***	17.68 (2.30,136.11)****	17.50 (2.27,134.71)***
Ν	high	1.32 (0.43,4.06)	1.31 (0.42,4.09)	1.10 (0.34,3.51)	1.47 (0.40,5.34)
	moderate	0.92 (0.33,2.60)	1.78 (0.50,6.35)	1.60 (0.44,5.82)	1.57 (0.43,5.69)
	low	1.46 (0.56,3.81)	2.23 (0.72,6.88)	1.99 (0.63,6.27)	1.98 (0.63,6.21)
	very low	1.18 (0.47,2.92)	1.68 (0.60,4.76)	1.66 (0.53,5.24)	1.38 (0.48,3.99)

*Table 4.* Risk ratios (RRs) for congestive heart failure associated with periodontitis and healthy periodontium, and monthly tomato consumption (MTC)

Y, yes periodontitis; N, no periodontitis.

\*Adjusted for age, race, gender, body mass index (BMI), smoking status, history of diabetes, hypertension, socioeconomic status and education level. <sup>†</sup>Adjusted for age, race, gender, BMI, waist to hip ratio, serum CRP, WBC count, smoking status, history of diabetes, hypertension, socioeconomic status, and education level.

<sup>‡</sup>Adjusted for age, race, gender, BMI, waist to hip ratio, serum CRP, WBC count, serum carotene, serum vitamin E, serum vitamin C, smoking status, history of diabetes, hypertension, socioeconomic status and education level.

<sup>§</sup>Adjusted for age, race, gender, BMI, waist to hip ratio, serum CRP, WBC count, serum carotene, serum vitamin E, serum vitamin C, smoking status, history of diabetes, hypertension, socioeconomic status, and education level and serum lycopene.

\*\*\**p* < 0.05, \*\*\*\**p* < 0.01.

Table 5. Risk ratios (RRs) for congestive heart failure associated with periodontitis and healthy periodontium, and serum lycopene (sLyco) levels

Periodontology status	SLyco quartiles	RR for CHF Y versus N (95% CI)*	RR for CHF Y versus N (95% CI) <sup>†</sup>	RR for CHF Y versus N (95% CI) <sup>‡</sup>	RR for CHF Y versus N (95% CI) <sup>§</sup>
Y	high	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
	moderate	0.71 (0.22,2.29)	0.72 (0.23,2.32)	0.64 (0.18,2.32)	0.64 (0.18,2.32)
	low	0.42 (0.15,1.22)	0.42 (0.14,1.21)	0.39 (0.12,1.28)	0.39 (0.12,1.28)
	very low	0.53 (0.18,1.59)	0.65 (0.21,2.03)	0.70 (0.19,2.52)	0.85 (0.22,3.21)
Ν	high	0.67 (0.16,2.87)	0.66 (0.15,2.82)	0.52 (0.11,2.39)	0.51(0.11,2.36)
	moderate	0.24 (0.07,0.81)**	0.25 (0.07,0.84)**	0.19 (0.05,0.69)**	0.19 (0.05,0.70)**
	low	0.71 (0.17,3.06)	1.04 (0.20,5.49)	0.83 (0.15,4.65)	0.56 (0.12,2.59)
	very low	0.62 (0.16,2.36)	0.59 (0.15,2.24)	0.57 (0.12,2.62)	0.59 (0.13,2.71)

Y, yes periodontitis; N, no periodontitis.

\*Adjusted for age, race, gender, body mass index (BMI), smoking status, history of diabetes, hypertension, socioeconomic status and education level. <sup>†</sup>Adjusted for age, race, gender, BMI, waist to hip ratio, serum CRP, WBC count, smoking status, history of diabetes, hypertension, socioeconomic status and education level.

<sup>‡</sup>Adjusted for age, race, gender, BMI, waist to hip ratio, serum CRP, WBC count, serum carotene, serum vitamin E, serum vitamin C, smoking status, history of diabetes, hypertension, socioeconomic status and education level.

<sup>§</sup>Adjusted for age, race, gender, BMI, waist to hip ratio, serum CRP, WBC count, serum carotene, serum vitamin E, serum vitamin C, smoking status, history of diabetes, hypertension, socioeconomic status, and education level and monthly tomato intake. \*\*p < 0.05,

ing high levels of other antioxidants. A sufficient supply of antioxidants from the diet might help prevent or delay the occurrence of pathological changes associated with oxidative stress (Giugliano 2000).

It has also been proposed that high levels of reactive oxygen species promote progression of periodontal disease. This may be a result of relatively low levels of superoxide dismutase and catalase in the tissues (Ellis et al. 1998). The beneficial effects of lycopene may be a result of lowering gingival tissue free radical concentrations, arresting disease progression.

Lycopene appears to be the most effective carotenoid in reducing both human aortic endothelial cell adhesion to monocytes and expression of adhesion molecules on the cell surface (Martin et al. 2000). An inverse relationship between plasma lycopene concentrations and CCA-IMT in Finnish males has been reported (Rissanen et al. 2000), and it was concluded that low plasma lycopene concentrations was associated with early atherosclerosis, manifested as increased CCA-IMT (Rissanen et al. 2000). A direct relationship between periodontitis and carotid artery intima-media wall thickness (CCA- IMT) has been reported by the ARIC study (Beck et al. 2001). With coronary artery disease being the most common etiologic factor for left ventricular systolic dysfunction, the major symptom of CHF, reduction or maintenance of CCA-IMT could reduce CHF risk.

Taken together, our data confirms other data that periodontitis may have systemic sequelae, as serum levels of CRP and WBC count were both elevated in individuals with periodontitis. We theorize that a relationship exists between periodontitis and elevated CHF risk, and that higher MTC reduced this risk in periodontitis subjects. CRP levels and WBC count were reduced in individuals with higher sLyco levels and higher MTC levels, respectively. The current observations may explain the epidemiologic links between tomato consumption and incidence of inflammatory diseases and explain the hypothesis that diets rich in antioxidants reduce the risk of CHF in individuals with periodontitis.

#### References

- Agarwal, S. & Rao, A. (1998) Tomato lycopene and low density lipoprotein oxidation: a human dietary intervention study. *Lipids* 33, 981–984.
- Agarwal, S. & Rao, A. (2000) Tomato lycopene and its role in human health and chronic diseases. *Canadian Medical Association Journal* 163, 739–744.
- Arbes, S. Jr., Slade, G. & Beck, JD. (1999b) Association between extent of periodontal attachment loss and self-reported history of heart attack: an analysis of NHANES III data. *Journal of Dental Research* 78, 1777– 1782.
- Beck, J., Elter, J., Heiss, G., Couper, D., Mauriello, S. & Offenbacher, S. (2001) Relationship of periodontal disease to carotid artery intima-media wall thickness: the atherosclerosis risk in communities (ARIC) study. Arteriosclerosis Thrombosis and Vascular Biology 21, 1816–1822.
- Beck, J., Offenbacher, S., Williams, R., Gibbs, P. & Garcia, R. (1998) Periodontitis: a risk factor for coronary heart disease. *Annals of Periodontology* 3, 127–141.
- Berk, B., Weintraub, W. & Alexander, R. (1990) Elevation of C-reactive protein in "active" coronary artery disease. *American Journal of Cardiology* 65, 168–172.
- Carlos, J., Wolfe, M. & Kingman, A. (1986) The extent and severity index: a simple method for use in epidemiologic studies of periodontal disease. *Journal of Clinical Periodontology* 13, 500–505.
- Carroll, Y., Corridan, B. & Morrissey, P. (2000) Lipoprotein carotenoid profiles and the susceptibility of low density lipoprotein to oxidative modification in healthy elderly volunteers. *European Journal of Clinical Nutrition* 54, 500–507.
- Chopra, M., O'Neill, M., Keogh, N., Wortley, G., Southon, S. & Thurnham, D. (2000) Influence of increased fruit and vegetable intake on plasma and lipoprotein carotenoids and LDL oxidation in smokers and nonsmokers. *Clinical Chemistry* 46, 1818–1829.
- Ellis, S., Tucci, M., Serio, F. & Johnson, R. (1998) Factors for progression of periodontal disease. *Journal of Oral Pathology and Medicine* 27, 101–105.
- Ezzati, T., Massey, J., Waksberg, J., Chu, A. & Maurer, K. (1992) Sample Design: Third National Health and Nutrition Examination Survey. Vital Health Statistics 2 113, 1–35.

- Forrester, J., Merz, C., Bush, T., Cohn, J., Hunninghake, D. & Parthasarathy, S. (1996) 27th Bethesda Conference: matching the intensity of risk factor management with the hazard for coronary heart disease events. *Journal of the American College of Nutrition* 27, 996–1006.
- Fowler, E., Breault, L. & Cuenin, M. (2001) Periodontal disease and its association with systemic disease. *Military Medicine* 166, 85–89.
- Fuhrman, B., Elis, A. & Aviram, M. (1997) Hypercholesterolemic effect of lycopene and beta-carotene is related to suppression of cholesterol synthesis and augmentation of LDL receptor activity in macrophages. *Biochemistry and Biophysical Research Communications* 233, 658–662.
- Fuhrman, B., Volkova, N., Rosenblat, M. & Aviram, M. (2000) Lycopene synergistically inhibits LDL oxidation in combination with vitamin E, glabridin, rosmarinic acid, carnosic acid, or garlic. *Antioxidant Redox Signaling* 2, 491–506.
- Genco, R., Offenbacher, S. & Beck, J. (2002) Periodontal disease and cardiovascular disease. Epidemiology and possible mechanisms. *Journal of the American Dental Association* 133, 14S–22S.
- Gerster, H. (1997) The potential role of lycopene for human health. Journal of the American College of Nutrition 16, 109–126.
- Giugliano, D. (2000) Dietary antioxidants for cardiovascular prevention. *Nutrition Metabolism and Cardiovascular Diseases* **10**, 38–44.
- Grossi, S. & Genco, R. (1998) Periodontal disease and diabetes mellitus: a two way relationship. *Annals of Periodontology* 3, 51–61.
- Haraszthy, V., Zambon, J., Trevisan, M., Zeid, M. & Genco, R. (2000) Identification of periodontal pathogens in atheromatous plaques. *Journal of Periodontology* **71**, 1554–1560.
- Herzberg, M., Brintzenhofe, K. & Clawson, C. (1983) Aggregation of human platelets and adhesion of Streptococcus sanguis. *Infection* and Immunity **39**, 1457–1469.
- Herzberg, M. & Meyer, M. (1996) Effects of oral flora on platelets: possible consequences in cardiovascular disease. *Journal of Periodontology* 67, 1138–1142.
- Kannel, W., Anderson, K. & Wilson, P. (1992) White blood cell count and cardiovascular disease. Insights from the Framingham study. *JAMA* 267, 1253–1256.
- Kinane, D. & Marshall, G. (2001) Periodontal manifestations of systemic disease. *Australian Dental Journal* 46, 45–48.
- Klipstein-Grobusch, K., Launer, L., Geleijnse, J., Boeing, H., Hofman, A. & Witteman, J. (2000) Serum carotenoids and atherosclerosis. The Rotterdam Study. *Atherosclerosis* 148, 49–56.
- Kohlmeier, L., Kark, J., Gomez-Gracia, E., Martin, B., Steck, S., Kardinaal, A., Ringstad, J., Thamm, M., Masaev, V., Riemersma, R., Martin-Moreno, J., Huttunen, J. & Kok, F. (1997) Lycopene and myocardial infarction risk in the EURAMIC Study.

American Journal of Epidemiology 146, 618–626.

- Liuizzo, G. & Rizello, V. (2001) C-reactive protein and primary prevention of ischemic heart disease. *Clinical Chimica Acta* 311, 45–48.
- Loos, B. G., Craandijk, J., Hoek, F. J., Wertheim-van Dillen, P. M. & van der Velden, U. (2000) Evaluation of systemic markers related to cardiovascular disease in peripheral blood of periodontitis patients. *Journal of Periodontology* **71**, 1528–1534.
- Martin, K., Wu, D. & Meydani, M. (2000) The effect of carotenoids on the expression of cell surface adhesion molecules and binding of monocytes to human aortic endothelial cells. *Atherosclerosis* 150, 265–274.
- Maseri, A., Biasucci, L. & Liuzzo, G. (1996) Elevated levels of interleukin-6 in unstable angina. *Circulation* 94, 874–877.
- Mayne, S. (1996) Beta-carotene, carotenoids, and disease prevention in humans. *FASEB Journal* 10, 690–701.
- Mendall, M. A., Patel, P., Ballam, L., Strachan, D. & Northfield, T. C. (1996) C reactive protein and its relation to cardiovascular risk factors: a population based cross sectional study. *BMJ* 312, 1061.
- National Heart, Lung and Blood Institute (September 1996) www.nhlbi.nih.gov/health/ public/heart/other/CHF.htm.
- Phillips, A., Neaton, J., Cook, D., Grimm, R. & Sharper, A. (1992) Leukocyte count and risk of major coronary heart disease events. *American Journal of Epidemiology* 136, 59–70.
- Rao, A. & Agarwal, S. (2000) Tomato lycopene and its role in human health and chronic diseases. CMAJ 163, 739–744.
- Ridker, P., Buring, J., Shih, J., Matais, M. & Hennekens, C. (1999) Prospective study of C-reactive protein and the risk of future cardiovascular events among apparently healthy women. *Circulation* 104.
- Ridker, P. M., Hennekens, C. H., Buring, J. E. & Rafai, N. (2000a) C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. *New England Journal of Medicine* 342, 836.
- Ridker, P. M., Rifai, N., Stampfer, M. J. & Hennekens, C. H. (2000b) Plasma concentration of interleukin-6 and the risk of future myocardial infarction among apparently healthy men. *Circulation* **101**, 1767.
- Rissanen, T., Voutilainen, S., Nyyssonen, K., Salonen, R. & Salonen, J. (2000) Low plasma lycopene concentration is associated with increased intima-media thickness of the carotid artery wall. *Arteriosclerrosis Thrombosis and Vascular Biology* 20, 2677–2681.
- Slade, G., Offenbacher, S., Beck, J., Heiss, G. & Pankow, J. (2000) Acute-phase inflammatory response to periodontal disease in the U.S. population. *Journal of Dental Research* 79, 49–57.
- Taylor, G. (2001) Bidirectional interrelationships between diabetes and periodontal diseases: an epidemiologic perspective. *Annals* of *Periodontology* **6**, 99–112.

#### 580 Wood & Johnson

- United States Department of Health and Human Services (USDHHS) (1996a) Third National Health and Nutrition Examination Survey, 1988–1994, NHANES III Household Adult Data File (CD-ROM). Public Use Data File. Documentation Number 76200. Hyattsville, MD: National Centre for Health Statistics.
- United States Department of Health and Human Services (USDHHS) (1996b) Third National Health and Nutrition Examination Survey, 1988–1994, NHANES III Household Adult Data File (CD-ROM). Public Use Data File. Documentation Number 76300. Hyattsville, MD: National Centre for Health Statistics.
- United States Department of Health and Human Services (USDHHS) (1996c) Third National Health and Nutrition Examination Survey, 1988–1994, NHANES III Laboratory Data File Documentation. Hyattsville, MD: National Centre for Health Statistics.
- Upritchard, J., Sutherland, W. & Mann, J. (2000) Effect of supplementation with tomato juice, vitamin E, and vitamin C on LDL oxidation and products of inflammatory activity in type 2 diabetes. *Diabetes Care* **23**, 733–738.
- Wu, T., Trevisan, M., Genco, R., Falkner, K., Dorn, J. & Sempos, C. (2000a) Examination of the relationship between periodontal health status and cardiovascular risk factors:

serum total and high density lipoprotein cholesterol, C-reactive protein, and plasma fibrinogen. *American Journal of Epidemiology* **151**, 273–282.

#### Address:

Nelson Wood Department of Periodontics University of Mississippi Medical Center 2500 North State Street Jackson, MS 39216-4505, USA Fax: +601 984 6120 E-mail: nwood@sod.umsmed.edu This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.