Determinants of Inflammatory Markers in a Bi-ethnic Population

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Background: Inflammation is a common pathophysiological pathway for a number of chronic diseases, and is strongly influenced by sociodemographic factors and lifestyle. Less is known about factors that may influence the inflammatory response in individuals of distinct ethnic backgrounds. Therefore, this study examined the relationship between ethnicity and blood levels of inflammatory markers in a sample of non-smoking church-goers.

Methods: In a cross-sectional investigation, 508 men and women (>35 years old, 62% White, 38% Black) participated in the Biopsychosocial Religion and Health substudy of the Adventist Health Study 2. The contribution of socioeconomic status (education level and difficulty meeting expenses for basic needs) and health covariates (exercise, vegetarian or other type of diet, body mass index, and presence of inflammatory conditions) toward serum levels of C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) was assessed with linear regression models. Levels of interleukin-10 (IL-10), an anti-inflammatory marker, were also assessed.

Results: Blacks showed higher levels of CRP and IL-6 than Whites. Controlling for sociodemographic and health variables attenuated the ethnic difference in CRP while IL-6 levels remained higher in Blacks than in Whites (β=.118; 95% confidence interval=.014–.206; *P*=.025). Ethnic differences in IL-10 and TNF-α were not found. Vegetarian diet was associated with lower CRP levels while exercise frequency was associated with higher IL-10 levels.

Conclusion: Higher susceptibility of Blacks to inflammatory diseases may reflect higher IL-6, which could be important in assessing health disparities among Blacks and Whites. Vegetarian diet and exercise may counteract effects of disparities. (*Ethn Dis.* 2011;21(2):142–149)

Key Words: Inflammatory Markers, Ethnicity, Health Behavior, Adventists

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Introduction

Ethnic differences in chronic disease incidence have been widely studied, with Blacks having a higher risk of hypertension, stroke and renal failure compared to Whites.[1] The reason for this disparity has not been completely elucidated but may be due to increased prevalence of disease risk factors among Blacks. Inflammation has been determined to be an important factor associated with chronic diseases, and is often indexed by elevated circulating levels of C-reactive protein (CRP) and pro-inflammatory cytokines.[2] Behavioral factors have a direct impact on inflammatory processes.[3]

The association between ethnicity and inflammation has been analyzed as well, showing that Blacks often have higher CRP than Whites.[4–6] Other inflammatory molecules include interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) which are associated with a pro-inflammatory response while IL-10 has anti-inflammatory effects.[7] Some studies have shown that Blacks have higher IL-6 levels than Whites,[6,8] but it is unclear whether IL-10 and TNF-α levels vary according to ethnic background.[8–10]

Ethnic specific differences in inflammation may have diverse determinants. For instance, low socioeconomic status (SES) has been associated with increased levels of CRP, IL-6 and TNF-α.[11–12] It is therefore possible that SES may partially explain why certain ethnicities are at higher risk for inflammatory problems. Health behavior factors also play a role in inflammation. Physical activity has been associated with lower circulating levels of CRP and IL-6 in both healthy and patient populations[13] and has been shown to increase concentrations of anti-inflammatory cytokines (such as IL-1 receptor antagonist and IL-10) to lower the inflammatory response.[14] In addition, diets rich in fruits, vegetables, whole grains and nuts have been associated with reductions in CRP and IL-6 levels, while diets high in red meat and high fat dairy have been directly correlated with increased inflammation.[15–16]

Among other lifestyle factors, alcohol consumption has been associated with lower levels of CRP among moderate drinkers compared to non-drinkers and heavy drinkers, a U-shaped pattern.[17–18] Cigarette smoking has been found to be a potent risk factor for increased levels of low-grade inflammation based on elevated CRP and IL-6 levels.[19–20]

One of the populations in which determinants of chronic disease have been studied is Seventh-day Adventists, a conservative religious group whose members normally abstain from alcohol and tobacco.[21–22] Thus, the population avoids some of the major identified factors involved in increasing inflammation and may provide the opportunity to illuminate the role of other factors, including ethnicity and lifestyle variables. In our study, ethnic differences in inflammation were assessed among a population of church-going Adventists. We also determined whether the ethnicity-inflammation relationship is affected by demographic, SES, behav-

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ioral or health status variables. The inflammatory markers that were analyzed include both pro-inflammatory (IL-6 and TNF-α) and anti-inflammatory (IL-10) cytokines as well as an acute phase protein (CRP).

METHODS

Study Population

This study was a cross-sectional analysis of the data gathered from a substudy of the Adventist Health Study-2 (AHS-2) referred to as the Biopsychosocial Religion and Health Study (BRHS).[23] Approximately 20,000 participants randomly selected from the 96,000 case AHS-2 sample were sent a 20-page religion and health questionnaire, and about 11,000 returned the questionnaire. The data collection began in September 2006 and was largely completed by August 2007. The study population consisted mainly of Black and White, Seventh-day Adventist males and females who were aged ≥35 years. In addition to completing the questionnaire, 508 BRHS participants also attended study-specific clinics in Loma Linda, Riverside, or Los Angeles to be assessed for biologic indicators and anthropometric measurements. Cytokine analysis was based on fasting blood samples provided by the participants on the day they attended the clinic. The institutional review board at Loma Linda University approved the study protocol, and informed consent was obtained from all participants.

Measurement of Variables

Sociodemographic Variables

Sociodemographic variables included age, sex, and ethnicity. Ethnicity was coded as Black or White based on self-report. Ethnicity was divided into Black (Black/African American, West Indian/Caribbean, African or other Black) and White (White non-Hispanic, Hispanic, Middle Eastern, Asian, Native Hawaiian/other Pacific Islander or American Indian) in the current analysis.

Socioeconomic Status

Socioeconomic status was assessed based on the participants' highest level of education as well as the degree of difficulty meeting family expenses for basic needs in the last year. Education was categorized as follows: a) grade school or some high school, b) high school or trade school diploma, c) some college, an Associate's degree, or a Bachelor's degree, and d) a Master's or Doctoral degree. The response choices for assessing the degree of difficulty meeting family expenses were: not at all, a little, somewhat, fairly, and very.

Health Behavior Variables

Behavioral variables included exercise, vegetarian diet, smoking, and alcohol consumption. Exercise was measured by the number of times per week that the participant engaged in regular vigorous activities using previously validated questions.[24–25] A 14-item food frequency questionnaire was used to assess the participants' dietary intake, and vegetarian status was assessed by whether or not participants consumed red meats, turkey or chicken, or fish over the last 12 months as three separate questionnaire items. A score of 1 indicated that participants never or rarely consumed the food items mentioned above, and a score of 2 indicated that participants consumed any of these foods at least 1 time per month. All values of 1 were coded as vegetarians, and all values of 2 were coded as non-vegetarians. Since there was only 1 current smoker and 18 participants who consumed alcohol more than 1 time per week, we did not control for these variables in the final analysis. Results did not change substantially when analyses were run with alcohol and smoking included as control variables (data not shown).

Health Status Variables

The participants' health status was assessed based on their height, weight, waist circumference, and calculated BMI as well as the presence of inflammatory conditions. Waist circumference was measured midway between the lower rib margin and the iliac crest to the nearest millimeter. Waist circumference measurements were not controlled for in the final regression analysis because of their high degree of correlation with BMI (r=.729; P=.000). The participants were assessed for the presence of a disease associated with inflammation based on whether or not they reported any of the following conditions: type 2 diabetes, stroke, transient ischemic attack, angina pectoris, rheumatoid arthritis, or sleep apnea.

Inflammatory Markers

Serum concentrations of CRP, IL-6, IL-10 and TNF-α were assessed based on fasting blood samples provided by participants that were processed and stored in −70°C freezers until they were ready to be tested. These inflammatory markers were measured in duplicate by enzyme linked immunosorbent assay (ELISA) kits from Assaypro (CRP), R & D Systems (IL-6), and ThermoScientific (IL-10 and TNF-α). The minimum detectable concentrations were 100 pg/mL for CRP, .039 pg/mL for IL-6, 3 pg/mL for IL-10, and 2 pg/mL for TNF-α. The intra-assay and inter-assay coefficient of variation (CV) were 5.5% and 7.6% for CRP, 6.9% and 7.2% for IL-6, 8.7% and 9.4% for IL-10, and 4.2% and 5.2% for TNF-α. All ELISA kits used were specific for the measurement of natural human CRP, IL-6, IL-10 and TNF-α concentrations in serum, and did not cross-react with other cytokine molecules. Standard ELISA plate readers were used to measure the absorbance of each sample.

Statistical Analysis

All statistical analysis was performed using SPSS (version 17). Ethnic differences in the study characteristics were determined using independent t tests for continuous variables or chi-square tests

Table 1. Main characteristics of the study population according to ethnicity

Factor	Whites (*n*=314)	Blacks (*n*=191)	*P* (Whites vs Blacks)	Total Population (*n*=505)
Age in years, Mean (SD)	71.4 (11.6)	64.4 (10.1)	.000	68.8 (11.6)
Sex, *n* (%)				
Male	128 (41.0)	58 (30.5)		186 (37.1)
Female	184 (59.0)	132 (69.5)	.018	316 (62.9)
Education, *n* (%)				
Grade school or some high school	5 (1.6)	5 (2.7)		10 (2.0)
High school or trade school diploma	11 (3.5)	19 (10.1)		30 (6.0)
Some college, Associate's or Bachelor's degree	146 (47.1)	124 (66.0)		270 (54.2)
Master's or Doctoral degree	148 (47.7)	40 (21.3)	.000	188 (37.8)
Difficulty meeting family expenses for basic needs in last year, *n* (%)				
Not at all	264 (85.2)	138 (74.6)		402 (81.2)
A little	26 (8.4)	25 (13.5)		51 (10.3)
Somewhat	8 (2.6)	6 (3.2)		14 (2.8)
Fairly	6 (1.9)	10 (5.4)		16 (3.2)
Very	6 (1.9)	6 (3.2)	.043	12 (2.4)
Alcohol consumption within the last 12 months, *n* (%)				
Consumed 3 drinks or less per month	299 (95.5)	187 (97.9)		486 (96.4)
Consumed 4 drinks per month or more	14 (4.5)	4 (2.1)	.163	18 (3.6)
Frequency of vigorous activities per week, *n* (%)				
Never or less than once per week	108 (36.4)	63 (35.4)		171 (36.0)
1–2 times per week	51 (17.2)	29 (16.3)		80 (16.8)
3–4 times per week	81 (27.3)	66 (37.1)		147 (30.9)
5 or more times per week	57 (19.2)	20 (11.2)	.048	77 (16.2)
Vegetarian Diet				
Non-vegetarian	152 (48.4)	137 (71.7)		289 (57.2)
Vegetarian	162 (51.6)	54 (28.3)	.000	216 (42.8)
BMI, mean (SD)	25.7 (4.7)	28.7 (5.9)	.000	26.8 (5.4)
Normal weight, *n* (%)	151 (48.1)	61 (31.9)		212 (42.0)
Overweight, *n* (%)	107 (34.1)	62 (32.5)		169 (33.5)
Obese, *n* (%)	56 (17.8)	68 (35.6)	.000	124 (24.6)
Diagnosed with any of the following conditions, *n* (%): Type 2 Diabetes, Stroke, TIA, Angina Pectoris, Rheumatoid Arthritis, Sleep Apnea				
No Disease Diagnosis	236 (75.2)	121 (65.4)		357 (71.5)
Diagnosed with Disease	78 (24.8)	64 (34.6)	.020	142 (28.5)

SD = standard deviation

for categorical variables (Table 1). In addition, Mann-Whitney tests were also used to determine the differences in inflammation between Blacks and Whites since the CRP, IL-6, IL-10 and TNF-values were not normally distributed and required log transformation before regression analysis could be performed (Table 2).

Multiple linear regression analysis was utilized to test the association between ethnicity and inflammation among the study population after controlling for demographic, socioeconomic, behavioral and health status variables. Separate models were utilized to test the effects of these variables on inflammation, and each model was analyzed in a stepwise fashion. Ethnicity was included in model 1, while model 2 added age, sex, education, and degree of difficulty meeting family expenses. Model 3 additionally added exercise and vegetarian diet consumption, and BMI was included in model 4. Model 5 added whether the participants were diagnosed with a medical condition. The serum concentrations of log transformed CRP, IL-6, TNF-α, and IL-10 served as continuous outcome variables in separate linear regression equations. Cytokine concentrations below the limit of detection were given a value of

Table 2. Ethnic differences in inflammatory marker concentrations

	Total population (*n*=493)	Whites (*n*=306)	Blacks (*n*=187)	*P* (Whites vs Blacks)
Inflammatory Marker Concentrations, Median (IQR)				
CRP (mg/mL)	.10 (.04–.24)	.09 (.04–.21)	.12 (.05–.29)	.010
IL-6 (pg/mL)	2.72 (1.59–5.62)	2.34 (1.53–4.52)	3.37 (1.95–7.40)	.000
IL-10 (pg/mL)	5.38 (3.24–8.80)	5.11 (2.96–8.80)	5.83 (3.74–9.03)	.082
TNF-α (pg/mL)	.01 (.01–7.49)	.001 (.001–8.07)	.001 (.001–7.38)	.668

IQR = interquartile range, CRP = c-reactive protein, IL-6 = interleukin-6, IL-10 = interleukin 10, TNF-α = tumor necrosis factor alpha

.001 representing a near zero value as demonstrated in a previous study.[26] The regression analysis was based on standardized regression coefficient values as well as R^2 change values which were used to determine the amount of variability in inflammation explained by the predictor variables in each of the given models.

RESULTS

The study population characteristics and differences between Blacks and Whites are shown in Table 1. The mean age was 68.8 years (range: 36–102); 63% of the participants were women and 37% were Black. Black participants were younger, achieved a lower level of education, and had more difficulty meeting family expenses for basic needs in the last year. Blacks were also less likely to consume a vegetarian diet, and had a higher mean BMI and waist circumference (waist circumference data not shown). Table 2 shows that higher levels of CRP and IL-6 were present among Black participants compared to the White participants while IL-10 and TNF-α levels did not differ between the two groups.

Regression coefficients for the association of each predictor variable with serum concentrations of CRP and IL-6 are illustrated in Table 3 and 4, respectively. CRP levels were found to be significantly higher among Blacks than Whites, but this relationship was no longer significant after controlling for the demographic and SES variables in model 2. After controlling for all covariates, CRP levels were positively associated with age, being female, BMI, and being non-vegetarian (Table 3). IL-6 was positively associated with age, BMI, and being Black after controlling for all other factors. Increased exercise frequency was associated with a decrease in IL-6 levels, but this relationship was no longer significant after controlling for BMI (Table 4). Nevertheless, IL-10 was positively associated with exercise frequency after controlling for all other covariates (β=.147, *P*=.005).

The R^2 change values are provided in Table 3 and 4. A significant proportion of variability in CRP was explained by ethnicity (*P*=.047), age, gender, education, and difficulty meeting family expenses for basic needs (*P*=.000), health behavior variables (*P*=.000), and BMI (*P*=.000). Likewise, ethnicity (*P*=.011), age, sex, education, and difficulty meeting family expenses for basic needs (*P*=.003), health behavior variables (*P*=.047) and BMI (*P*=.003) also explained significant amounts of variability in IL-6 levels. Finally, health behavior variables (mainly exercise frequency) explained a significant proportion of IL-10 variability based on the regression analysis (R^2 change=.025; *P*=.006).

DISCUSSION

This study has shown that IL-6 may serve as an important ethnic-specific cytokine that is higher among Blacks than Whites, while the other inflammatory markers or anti-inflammatory marker (IL-10) did not differ between Blacks and Whites. Healthy lifestyle behaviors were associated with a lower inflammatory status, after controlling for ethnic differences, as increased exercise frequency was associated with increased IL-10 levels, and consumption of a vegetarian diet was associated with lower CRP levels.

The present study provides further evidence of an association between ethnicity and inflammation, in line with other studies that have found higher IL-6 levels among Blacks compared to Whites.[8,27,28] However, these studies did not control for variables such as diet or exercise when assessing the ethnic differences in IL-6, and may have been confounded by differences between Blacks and Whites in regard to lifestyle induced changes in inflammation. Earlier study designs were also based on a

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Table 3. Regression analysis models illustrating the association between various predictor variables and CRP

Factor	Model 1			Model 2			Model 3			Model 4			Model 5		
	β	B (SE)	*P*	β	B (SE)	*P*	β	B (SE)	*P*	β	B (SE)	*P*	β	B (SE)	*P*
Ethnicity															
Blacks vs Whites	.096	.108 (.054)	.047	.093	.105 (.057)	.067	.060	.068 (.057)	.230	−.008	−.009 (.054)	.866	−.009	−.011 (.055)	.847
Age				.108	.005 (.002)	.029	.101	.005 (.002)	.040	.129	.006 (.002)	.006	.126	.006 (.002)	.009
Sex															
Females vs males				.175	.193 (.054)	.000	.172	.190 (.053)	.000	.183	.202 (.050)	.000	.184	.203 (.051)	.000
Education				−.059	−.049 (.042)	.247	−.008	−.007 (.043)	.875	−.001	−.001 (.040)	.979	−.001	.000 (.040)	.991
Difficulty meeting family expenses in the last year				.009	.006 (.029)	.845	.006	.003 (.028)	.904	−.005	−.003 (.027)	.902	−.006	−.004 (.027)	.893
Frequency of vigorous activities per week							−.110	−.026 (.011)	.022	−.059	−.014 (.011)	.197	−.058	−.013 (.011)	.207
Vegetarian diet vegetarian vs non-vegetarian							−.170	−.185 (.053)	.000	−.108	−.118 (.051)	.020	−.107	−.117 (.051)	.023
Body mass index										.344	.036 (.005)	.000	.341	.036 (.005)	.000
Inflammatory condition diagnosis disease vs no disease													.012	.014 (.057)	.803
R^2 Change	.009			.048			.039			.102			.000		

β = standardized regression coefficient, B = unstandardized regression coefficient, SE = standard error

much smaller sample size than was used for the current investigation.

Adipose tissue synthesizes inflammatory markers such as IL-6, and increased body mass has been associated with higher inflammation levels among Blacks.[29,30] However, the ethnic specific difference in IL-6 was significant even after controlling for BMI in the current study, so other factors may be responsible for this relationship. One possible reason for the ethnic variations in the level of this cytokine is due to differences in cytokine gene polymorphisms. It has been suggested that specific allelic variations in the regulatory regions of inflammatory cytokine genes may alter the expression of some cytokines.[31] One of the genotypes that results in high IL-6 production (G/G IL-6 genotype) has been predominantly found in Blacks, and may explain higher levels of this cytokine among this ethnic group.[32]

Although there were higher CRP levels among Blacks in the present study, this association was no longer significant after controlling for the other covariates. Studies among the US population have shown that there are higher CRP levels among Blacks in relation to Whites.[33–35] However, like the results from the present study, the ethnicity-CRP association found in some of the investigations ultimately disappeared after controlling for various health-related factors.[36–37] In the current study, the ethnicity-CRP relationship was largely attenuated after controlling for vegetarian diet consumption as well as exercise frequency, and even more attenuated after controlling for BMI. Therefore, future studies should investigate lifestyle components as well as other variables associated with obesity that may serve as important mediating factors between ethnicity and CRP.

No significant differences in IL-10 and TNF-α levels were found between Black and White patients in the present study. Although lower levels of IL-10 among Blacks compared to Whites have been reported previously,[9] the analysis

Table 4. Regression analysis models illustrating the association between various predictor variables and IL-6

Factor	Model 1			Model 2			Model 3			Model 4			Model 5		
	β	B (SE)	*P*	β	B (SE)	*P*	β	B (SE)	*P*	β	B (SE)	*P*	β	B (SE)	*P*
Ethnicity															
Blacks vs Whites	.122	.113 (.044)	.011	.165	.153 (.047)	.001	.154	.143 (.047)	.003	.124	.115 (.048)	.016	.121	.113 (.048)	.020
Age				.180	.007 (.002)	.000	.163	.006 (.002)	.001	.175	.007 (.002)	.000	.167	.006 (.002)	.001
Sex															
Females vs Males				−.005	−.004 (.045)	.924	−.017	−.015 (.045)	.732	−.012	−.011 (.044)	.805	−.010	−.009 (.045)	.843
Education				−.072	−.049 (.035)	.157	−.050	−.034 (.036)	.338	−.047	−.032 (.035)	.363	−.045	−.031 (.035)	.383
Difficulty meeting family expenses in the last year				−.042	−.021 (.024)	.388	−.044	−.022 (.024)	.356	−.049	−.024 (.024)	.303	−.051	−.025 (.024)	.290
Frequency of vigorous activities per week							−.116	−.022 (.009)	.018	−.094	−.018 (.009)	.055	−.091	−.017 (.009)	.063
Vegetarian diet vegetarian vs nonvegetarian							−.029	−.026 (.044)	.556	−.003	−.002 (.044)	.957	.001	.001 (.045)	.988
Body mass index										.147	.013 (.004)	.003	.141	.012 (.004)	.006
Inflammatory condition diagnosis disease vs no disease													.030	.030 (.050)	.554
R^2 Change	.015			.036			.014			.019			.001		

β = standardized regression coefficient, B = unstandardized regression coefficient, SE = standard error

was based on stimulated peripheral blood samples rather than basal cytokine levels in the blood. Therefore, no direct evidence of ethnic differences in circulating IL-10 levels was shown. As far as ethnic differences in TNF-α are concerned, the results are mixed. A study by Kalra et al[8] found that TNF-α levels were higher among Blacks in relation to Whites from the United Kingdom, while Elkind et al[10] found no significant difference in TNF-α levels among Blacks and Whites from the United States. Therefore, geographic location, environmental factors, and other variables such as diet, exercise and body mass may play an important role in the onset of inflammation among different ethnic groups.

Based on the results provided, engaging in exercise and consuming a vegetarian diet was associated with lower inflammation levels. Vegetarians demonstrated a lower blood concentration of CRP compared to non-vegetarians which is in accordance with previous research showing that long-term vegetarians have a lower risk of coronary heart disease and an improved antioxidant and inflammatory status compared to non-vegetarians.[38] In addition, greater amounts of regular physical activity have been associated with elevated IL-10 levels in healthy older males,[39] and aerobic exercise training has been reported to exert anti-inflammatory effects in type 2 diabetics due to increases in IL-10 concentrations.[40] Specifically, high intensity exercise has been more strongly associated with increased IL-10 levels when compared to moderate and light intensity exercises among healthy, well-trained participants,[41] suggesting that more vigorous exercise may provide stronger anti-inflammatory effects.

Strengths and Limitations

This study assessed pro-inflammatory and anti-inflammatory cytokines that were not examined together in previous studies. The absence of cigarette smokers and low amount of alcohol con-

sumption allowed the confounding effects of smoking and excess alcohol on inflammatory markers to be avoided. Finally, the current study sample size provided sufficient power for detecting associations between the study variables.

This was a cross-sectional study so causality between ethnicity and other variables and levels of inflammatory markers cannot be assumed. There were differences in baseline factors between Blacks and Whites. We adjusted for these factors, but residual confounding may remain due to the effects of other variables not measured in the present study (such as lean body mass differences between Blacks and Whites) as well as incomplete statistical adjustment. However, abdominal fat content was assessed by waist circumference which showed the same ethnic specific differences found based on BMI measurements.

The study population consisted of only Adventist church goers and generalizability to the larger population may be limited. Genetic markers of the inflammatory cytokines were not examined, limiting our analysis to cytokine concentrations rather than specific gene activity. The TNF-α concentration of 204 of the study participants (63% White and 37% Black) was below the limit of detection as well, similar to the proportion of Whites and Blacks in the overall study. It is possible that this population of church goers may have been less susceptible to increased inflammation based on their overall health and lifestyle practices, making it difficult to detect this inflammatory marker. Therefore, future analysis of inflammation using TNF-receptor 1 as a surrogate marker for TNF-α may be preferable since TNF-α has a short half-life ($\sim$15 minutes) and can be difficult to detect among certain populations using standard ELISA kits.[42]

CONCLUSION

Inflammatory based risk for health problems may vary according to ethnicity and other demographic factors. Yet inflammation levels also seem to be influenced by other variables such as diet, exercise, and overall body mass. Interventions that focus on improving these health behaviors may therefore be the key to reducing the risk for chronic diseases.

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REFERENCES

1. Kurian AK, Cardarelli KM. Racial and ethnic differences in cardiovascular disease risk factors: A systematic review. *Ethn Dis*. 2006; 16(1):143–152.
2. Reuben DB, Cheh AI, Harris TB, et al. Peripheral blood markers of inflammation predict mortality and functional decline in high-functioning community-dwelling older persons. *J Am Geriatr Soc*. 2002;50(4):638–644.
3. Kelishadi R, Mirghaffari N, Poursafa P, Gidding SS. Lifestyle and environmental factors associated with inflammation, oxidative stress and insulin resistance in children. *Atherosclerosis*. 2009;203(1):311–319.
4. Anand SS, Razak F, Yi QL, et al. C-reactive protein as a screening test for cardiovascular risk in a multiethnic population. *Arterioscler Thromb Vasc Biol*. 2004;24(8):1509–1515.
5. Kelley-Hedgepeth A, Lloyd-Jones DM, Colvin A, et al. Ethnic differences in C-reactive protein concentrations. *Clin Chem*. 2008; 54(6):1027–1037.
6. Walston JD, Fallin MD, Cushman M, Lange L, Psaty B, Jenny N, et al. IL-6 gene variation is associated with IL-6 and C-reactive protein levels but not cardiovascular outcomes in the Cardiovascular Health Study. *Hum Genet*. 2007;122(5):485–494.
7. Elenkov IJ. Neurohormonal-cytokine interactions: implications for inflammation, common human diseases and well-being. *Neurochem Int*. 2008;52(1–2):40–51.
8. Kalra L, Rambaran C, Chowienczyk P, et al. Ethnic differences in arterial responses and inflammatory markers in Afro-Caribbean and Caucasian subjects. *Arterioscler Thromb Vasc Biol*. 2005;25(11):2362–2367.
9. Kimball P, Elswick RK, Shiffman M. Ethnicity and cytokine production gauge response of patients with hepatitis C to interferon-alpha therapy. *J Med Virol*. 2001;65(3):510–516.
10. Elkind MS, Cheng JF, Boden-Albala B, et al. Tumor necrosis factor receptor levels are associated with carotid atherosclerosis. *Stroke*. 2002;33(1):31–37.
11. Gimeno D, Brunner EJ, Lowe GDO, Rumley A, Marmot MG, Ferrie JE. Adult socioeconomic position, C-reactive protein and interleukin-6 in the Whitehall II prospective study. *Eur J Epidemiol*. 2007;22(10):675–683.
12. Koster A, Bosma H, Penninx B, et al. Association of inflammatory markers with socioeconomic status. *J Gerontol A Biol Sci Med Sci*. 2006;61(3):284–290.
13. Plaisance EP, Grandjean PW. Physical activity and high-sensitivity C-reactive protein. *Sports Med*. 2006;36(5):443–458.
14. Petersen AMW, Pedersen BK. The anti-inflammatory effect of exercise. *J Appl Physiol*. 2005;98(4):1154–1162.
15. Lopez-Garcia E, Schulze MB, Fung TT, et al. Major dietary patterns are related to plasma concentrations of markers of inflammation and endothelial dysfunction. *Am J Clin Nutr*. 2004;80(4):1029–1035.
16. Nettleton JA, Steffen LM, Mayer-Davis EJ, et al. Dietary patterns are associated with biochemical markers of inflammation and endothelial activation in the Multi-Ethnic Study of Atherosclerosis (MESA). *Am J Clin Nutr*. 2006;83(6):1369–1379.
17. Albert MA, Glynn RJ, Ridker PM. Alcohol consumption and plasma concentration of C-reactive protein. *Circulation*. 2003;107(3): 443–447.
18. Pai JK, Hankinson SE, Thadhani R, Rifai N, Pischon T, Rimm EB. Moderate alcohol consumption and lower levels of inflammatory markers in US men and women. *Atherosclerosis*. 2006;186(1):113–120.
19. Wannamethee SG, Whincup PH, Rumley A, Lowe GDO. Inter-relationships of interleukin-6, cardiovascular risk factors and the metabolic syndrome among older men. *J Thromb Haemost*. 2007;5(8):1637–1643.
20. Helmersson J, Larsson A, Vessby B, Basu S. Active smoking and a history of smoking are associated with enhanced prostaglandin F-2 alpha, interleukin-6 and F-2-isoprostane formation in elderly men. *Atherosclerosis*. 2005;181(1):201–207.
21. Fraser GE, Shavlik DJ. Risk factors for all-cause and coronary heart disease mortality in the oldest-old - The Adventist Health Study. *Arch Intern Med*. 1997;157(19):2249–2258.
22. Butler TL, Fraser GE, Beeson WL, et al. Cohort profile: The Adventist Health Study-2 (AHS-2). *Int J Epidemiol*. 2008;37(2):260–265.
23. Lee JW, Morton KR, Walters J, et al. Cohort Profile: the biopsychosocial religion and health study (BRHS). *Int J Epidemiol*. 2009;38(6): 1470–1478.

24. Singh PN, Tonstad S, Abbey DE, Fraser GE. Validity of selected physical activity questions in white Seventh-day Adventists and non-Adventists. *Med Sci Sports Exerc*. 1996;28(8):1026–1037.
25. Singh PN, Fraser GE, Knutsen SF, Lindsted KD, Bennett HW. Validity of a physical activity questionnaire among African-American Seventh-day Adventists. *Med Sci Sports Exerc*. 2001;33(3):468–475.
26. Dhabhar FS, Burke HM, Epel ES, et al. Low serum IL-10 concentrations and loss of regulatory association between IL-6 and IL-10 in adults with major depression. *J Psychiatr Res*. 2009;43(11):962–969.
27. Mills PJ, von Kanel R, Natarajan L, Ziegler MG, Dimsdale JE. Inflammation and sleep in healthy individuals. *Sleep*. 2007;30(6):729–735.
28. Chapman BP, Khan A, Harper M, et al. Gender, race/ethnicity, personality, and interleukin-6 in urban primary care patients. *Brain Behav Immun*. 2009;23(5):636–642.
29. Mohamed-Ali V, Pinkney JH, Coppack SW. Adipose tissue as an endocrine and paracrine organ. *Int J Obes*. 1998;22(12):1145–1158.
30. Kelley-Hedgepeth A, Lloyd-Jones DM, Colvin A, et al. Ethnic differences in C-reactive protein concentrations. *Clin Chem*. 2008;54(6): 1027–1037.
31. Stowe RP, Peek MK, Cutchin MP, Goodwin JS. Plasma Cytokine Levels in a Population-Based Study: Relation to Age and Ethnicity. *J Gerontol A Biol Sci Med Sci*. 2009;65(4):429–433.
32. Delaney NL, Esquenazi V, Lucas DP, Zachary AA, Leffell MS. TNF-alpha, TGF-beta, IL-10, IL-6, and INF-gamma alleles among African Americans and Cuban Americans. Report of the ASHI Minority Workshops: Part IV. *Hum Immunol*. 2004;65(12):1413–1419.
33. Albert MA, Glynn RJ, Buring J, Ridker PM. C-reactive protein levels among women of various ethnic groups living in the United States - (from the Women's Health Study). *Am J Cardiol*. 2004;93(10):1238–1242.
34. Khera A, McGuire DK, Murphy SA, et al. Race and gender differences in C-reactive protein levels. *J Am Coll Cardiol*. 2005; 46(3):464–469.
35. LaMonte MJ, Durstine JL, Yanowitz FG, et al. Cardiorespiratory fitness and C-reactive protein among a tri-ethnic sample of women. *Circulation*. 2002;106(4):403–406.
36. McDade TW, Hawkley LC, Cacioppo JT. Psychosocial and behavioral predictors of inflammation in middle-aged and older adults: the Chicago health, aging, and social relations study. *Psychosom Med*. 2006;68(3):376–381.
37. Patel DA, Srinivasan SR, Xu JH, Li SX, Chen W, Berenson GS. Distribution and metabolic syndrome correlates of plasma C-reactive protein in biracial (Black-White) younger adults: the Bogalusa Heart Study. *Metabolism*. 2006;55(6):699–705.
38. Szeto YT, Kwok TCY, Benzie IFF. Effects of a long-term vegetarian diet on biomarkers of antioxidant status and cardiovascular disease risk. *Nutrition*. 2004;20(10):863–866.
39. Jankord R, Jemiolo B. Influence of physical activity on serum IL-6 and IL-10 levels in healthy older men. *Med Sci Sports Exerc*. 2004;36(6):960–964.
40. Kadoglou NPE, Iliadis F, Angelopoulou N, et al. The anti-inflammatory effects of exercise training in patients with type 2 diabetes mellitus. *Eur J Cardiovasc Prev Rehabil*. 2007;14(6):837–843.
41. Peake JM, Suzuki K, Hordern M, Wilson G, Nosaka K, Coombes JS. Plasma cytokine changes in relation to exercise intensity and muscle damage. *Eur J Appl Physiol*. 2005; 95(5–6):514–521.
42. Schroder J, Stuber F, Gallati H, Schade FU, Kremer B. Pattern of soluble TNF receptor-I and receptor-II in sepsis. *Infection*. 1995; 23(3):143–148.

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