

ARIC Manuscript Proposal #724

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1.a. Full Title: Trait anger and carotid atherosclerosis: Examination of a possible mechanism in cardiovascular disease. The Atherosclerosis Risk in Communities (ARIC) Study

1.b. Abbreviated title (Length 26 characters): Trait anger - IMT

2. Writing Group (List the individual with lead responsibility first):

Lead: Janice E. Williams

Bank of America Center

137 E. Franklin St., Suite 306

Chapel Hill, NC 27514

Telephone: 919-966-1967

Fax: 919-966-9800

E-mail: jwill22@bellsouth.net

Aaron Folsom, Catherine Paton, Javier Nieto, David Couper, Al Tyroler

3. Timeline: Complete data analysis – August 2000

Draft of manuscript to Publications Committee – December 2000

Journal submission – April 2001

Hypothesis:

1. Proneness to anger as a personality trait (trait anger) is positively associated with carotid atherosclerosis independent of the standard CVD risk factors.
2. Proneness to anger as a personality trait is positively associated with the progression of carotid atherosclerosis independent of the standard CVD risk factors.

4. Rationale:

Previous studies in ARIC and elsewhere have shown a positive association between anger and clinically manifest disease, e.g., CHD (1-4) and stroke (5, 6). However, the mechanism by which anger influences these disease states is unknown. The two most-often articulated explanatory hypotheses, relative to CHD at least, implicate anger either as a “trigger” of physiologic events that culminate in occlusive thrombosis (7) or as a factor in atherogenesis via the heightened sympathetic arousal and catecholamine secretion associated with the anger experience (8). The purpose of the proposed study is to examine the hypothesis that anger may be an important factor in the process of atherosclerosis. To do so, we will examine both the cross-sectional and prospective association between trait anger and intima-medial wall thickness (IMT), controlling for the established CVD risk factors. IMT is regarded as a proxy for diffuse or generalized atherosclerosis (9, 10), although this claim is not universally supported (11). Observational studies, including those from ARIC, have reported a positive association

between IMT and prevalent CVD among middle-aged adults (10), as well as between IMT and incident CHD (9) and stroke (12).

Three studies of the relationship between anger and atherosclerosis are found in the literature. In prospective analyses, Julkunen, Salonen, Kaplan et al. (13) found a near two-fold increase in the acceleration of carotid atherosclerosis (as measured by intima-medial wall thickness) among angry and cynically distrustful Finnish men. In cross-sectional analyses, Matsumoto, Uyama, Shimizu et al. (14) reported that ease of anger arousal was positively associated with the severity of carotid atherosclerosis (as measured by plaque scores) in Japanese men and women. In a more recent cohort study, higher levels of trait anger were correlated with higher levels of IMT among middle-aged women 10 years later, on average (15).

The results of the proposed study could contribute to a greater understanding of a mechanism by which stable personality attributes such as anger influence cardiovascular disease. ARIC provides the opportunity to investigate the anger-atherosclerosis hypothesis in a large population-based sample of both black and white men and women, a less restricted demographic representation than has been found in previous studies.

6. Data(variables, time window, source, inclusions/exclusions): Visit 1 - educational level, prevalent stroke, prevalent CHD; Visit 2 - age, gender, race/ethnicity, Spielberger Trait Anger Scale, LDL and HDL cholesterol levels, systolic BP, diastolic BP, fibrinogen, diabetes, waist-to-hip ratio, alcohol consumption, cigarette smoking, antihypertensive medication use, mean of the reader trend adjusted IMT variables (MNB45_1); Visit 3 - mean of the reader trend adjusted IMT variables (MNC45_1); Visit 4 – mean of the reader trend adjusted IMT variables (MND45_1).

Statistical analysis: The study hypotheses will be tested using multiple linear regression analysis. The outcome variable in the cross-sectional analyses will be IMT values at Visit 2; for the prospective analyses it will be mean change in IMT from Visit 2 to Visit 4. The following hierarchical models will be fit for each hypothesis:

Model 1: Crude

Model 2: Adjusting for age, gender, race/ethnicity

Model 3: Adjusting for age, gender, race/ethnicity, level of educational attainment, systolic and diastolic blood pressure levels, LDL- and HDL-cholesterol levels, diabetes, waist-to-hip ratio, alcohol intake, antihypertensive medication use, cigarette smoking, and fibrinogen.

Interaction tests will be performed to verify no interaction before fitting models 2 and 3.

Linear regression analysis will also estimate least square mean (and mean change) values of IMT by level of anger to determine whether higher levels of anger are associated with higher levels/greater increases in IMT.

Literature Cited

1. Hayne SG, Feinleib M, Kannel WB. The relationship of psychosocial factors to coronary heart

- disease in the Framingham study. III. Eight-year incidence of coronary heart disease. *Am J Epidemiol* 1980;111:37-58.
2. Mittleman MA, Maclure M, Sherwood JB, Mulry RP, Toffler GH, Jacobs SC, Friedman R, Benson H, Muller JE. Triggering of acute myocardial infarction onset by episodes of anger. *Circulation* 1995;7:1720-1725.
 3. Kawachi I, Sparrow D, Spiro A III, Vokonas P, Weiss ST. A prospective study of anger and coronary heart disease: the Normative Aging Study. *Circulation* 1996;94:2090-2095.
 4. Williams JE, Paton CC, Siegler IC, Eigenbrodt ML, Nieto FJ, Tyroler HA. Anger proneness predicts CHD risk: Prospective analysis from the Atherosclerosis Risk in Communities (ARIC) Study, *Circulation*, in press.
 5. Everson SA, Kaplan GA, Goldberg DE, Lakka TA, Sivenius J, Salonen JT. Anger expression and incident stroke: Prospective evidence from the Kuopio Ischemic Heart Disease Study. *Stroke* 1999;523-528.
 6. Williams JE, Nieto FJ, Paton CC, Couper DJ, Wyatt S, Tyroler HA. The Influence of frequent and intense anger on incident stroke: Findings from the Atherosclerosis Risk in Communities (ARIC) Study, under review.
 7. Mittleman MA, Maclure M, Sherwood JB, Mulry RP, Toffler GH, Jacobs SC, Friedman R, Benson H, Muller JE. Triggering of acute myocardial infarction onset by episodes of anger. *Circulation* 1995;7:1720-1725.
 8. Herd JA. Behavioral factors in the physiologic mechanisms of cardiovascular disease. In SM Weiss, JA Herd, & BH Fox (Eds.), *Perspectives in behavioral medicine*. New York: Academic Press, 1981:55-65.
 9. Chambless LE, Heiss G, Folsom AR, Rosamond W, Szklo M, Sharrett AR, Clegg LX. Association of coronary heart disease incidence with carotid arterial wall thickness and major risk factors: The Atherosclerosis Risk in Communities (ARIC) study, 1987-1993. *Am J Epidemiol* 1997;146:483-494.
 10. Burke GL, Evans GW, Riley WA, Sharrett AR, Howard G, Barnes RW et al. Arterial wall thickness is associated with prevalent cardiovascular disease in middle-aged adults: The Atherosclerosis Risk in Communities (ARIC) study. *Stroke* 1995;26:386-391.
 11. Adams MR, Nakagomi A, Keech A, Robinson J, McCredie R, Bailey BP, et al. Carotid intima-media thickness is only weakly correlated with the extent and severity of coronary artery disease. *Circulation* 1995;92:2127-2134.
 12. Bots ML, Hoes AW, Koudstaal PJ, Hofman A, Grobbee DE. Common carotid intima-media thickness and risk of stroke and myocardial infarction: The Rotterdam Study. *Circulation* 1997;96:1432-1437.
 13. Julkunen J, Salonen R, Kaplan GA, Chesney MA, Salonen JT. Hostility and the progression of carotid atherosclerosis. *Psychosom Med*. 1994;56:519-525.
 14. Matsumoto Y, Uyama O, Shimizu S, Michishita H, Mori R, Owadda T, Sugita M. Do anger and aggression affect carotid atherosclerosis? *Stroke*. 1993;24:983-986.
 15. Matthews KA, Owens JF, Kuller LH, Sutton-Tyrrell K, Jansen-McWilliams L. Are hostility and anxiety associated with carotid atherosclerosis in healthy postmenopausal women? *Psychosomatic Medicine* 1998;60:633-638.