1. Title:
Dietary Iron and Atherosclerosis

2. Writing Group:
(lead) Stolzenberg
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CC Representative

3. Timeline:
immediately

4. Rationale:
Previous studies have demonstrated relationships between Hb and several risk factors for cardiovascular
disease which include blood pressure (1), acute MI (1), serum cholesterol (2), body weight (3), cigarette
smoking (4), and physical activity. Hemoglobin may reflect in some respect iron adequacy as well as,
nutritional status. In addition, aortic tissue iron concentration has been associated with occlusive disease and
abdominal aneurysm (5). Although the mechanisms by which these effects are not understood, increased
wall stress, endothelial cell damage, free radical reactions, and altered collagen and elastin synthesis and
degradation are suggested as etiological factors (5). Theoretically, if iron absorption exceeds iron losses,
total body iron content will increase with age. Iron is a catalyst in the formation of hydroxyl radicals from
hydrogen peroxide. It has been suggested that iron metabolism in aortic tissue, independent of serum
hemoglobin, may contribute to lipid peroxidation and hence atherosclerosis (5). A suggested mechanism for
the hemoglobin-blood pressure association is blood viscosity and vascular resistance (6). Blood viscosity
increases logarithmically with a linear increase in hematocrit (6,7). Studies have not been done to assess the
association between dietary iron and atherosclerosis (subclinical and clinical manifestations).

5. Main Hypothesis:
Dietary iron is an independent risk factor for atherosclerosis.

6. Analysis and Data:
The analysis will examine the relationship between dietary iron and atherosclerosis adjusted for confounders.
Dietary iron as well as other dietary variables will be imputed from the baseline ARIC dietary intake form.
The outcome variable will be atherosclerosis measured by B-mode ultrasound and cardiovascular disease
events. Analysis will include distribution assessment, transformation, descriptive analysis, hypothesis testing,
assessment of confounding and effect modification. We will use multiple regression techniques to assess the
association.
Dependent Variables:
- Carotid distensibility data, carotid intima-media thickness (average of imputed values), prevalent cardiovascular vascular
disease events

Independent Variables:
- Dietary iron, hemoglobin, hematocrit
- Major cardiovascular risk factors...smoking history, blood pressure, lipids, age, sex, race

Other adjustment variables:
- Antioxidants (vitamin C, vitamin E, total carotenoids, beta carotene)
- Dietary fats (saturated fats, polyunsaturated fats, monounsaturated fats)
- Body mass index (height and weight)
- Folate, vitamin B12, vitamin B6
- Dietary sodium
- Total kcals
- Physical activity

REFERENCES:


