Title: Retinal Microvascular Abnormalities and Stroke/Lacunar Syndromes SLS -- The ARIC Study

Short Title: Retinal and Stroke/TIA

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Timeline:
Submit proposal to Publications Committee July, 1996
Develop algorithm for lacunar syndromes September, 1996
Complete analysis December, 1995
Submit first draft to publications committee February, 1997
Submit to journal April, 1997

Rationale:
The major risk factor for stroke/TIA is hypertension. However, a few blood pressure measurements taken in a research setting may not reflect the overall lifetime blood pressure status. In addition, the widespread use of anti-hypertensive medicine in the US further distorts the association. Retinal microvascular abnormalities associated with hypertension may provide a 'record' of elevated BIOS pressure reflective of intensity of exposure, its duration, and host susceptibility, and therefore add predictive power for identifying persons at increased risk for stroke/TIA.

Lacunar infarcts are small infarcts that lie in the deeper, noncortical parts of the cerebrum brainstem which result from the occlusion of penetrating branches of the large cerebral arteries. A striking loss of arteriolar architecture with fibrous replacement is the most frequently seen arterial lesion underlying lacunes (Fisher 1969). These lesions may be called fibrinoid necrosis or lipohyalinosis. Microatheromata may also be seen at the origin of their penetrating arteries. Thus, the underlying pathogenic process generally reflects unique degenerative changes in small arteries and arterioles rather than atherosclerosis in larger arteries.

Retinal arteries branch from brain arteries. The size of the arteries/arterioles involved in lacunes (40 to 200 microns) is very similar to the retinal arterioles associated by retinal photography (25 to 120 microns). In addition, the histology and pathology of retinal and cerebral small arteries are similar. Therefore, it is reasonable to posit that retinal microvascular changes are associated with lacunar infarcts.

A lacunar syndrome may be suggested by clinical examination. The classical lacunar syndromes are pure motor strokes, pure sensory stroke, sensorimotor stroke and ataxic hemiparesis. Although the TIA/Stroke questionnaire used in the ARIC Study was not designed specifically to ascertain lacunar syndromes, most information regarding lacunar syndromes is available from it. The proposed definition of lacunar syndromes in the ARIC Study is: a syndrome of unilateral motor or/and sensory deficit involving at least 2 of 3 areas (face, arm, leg). The presence of a visual field deficit evidence of big cerebral dysfunction (e.g., dysphasia, visuospatial disturbance or features that clearly localize the lesion in the vertebrobasilar distribution (e.g., crossed deficits, though not dysarthria) exclude the diagnosis of lacunar syndrome.
The TIA/Stroke questionnaire was administered to all the ARIC participants during the baseline, Visit 2 and Visit 3 examinations. At the third examination, a retinal photograph was taken on all participants (randomly sampled eye). An algorithmic definition of lacunar syndromes based on TIA/stroke questionnaire will be developed in this study.

Main Hypothesis:
1) Retinal microvascular abnormalities are associated with stroke/TIA defined by TIA/stroke questionnaire algorithm, at the population level.
2) Retinal microvascular abnormalities are more strongly associated with lacunar infarcts than non-lacunar infarcts, both types identified by means of the TIA/stroke questionnaire.

Data (variables, source, inclusion/exclusion):
Visit 3 retinal data, baseline, Visit 2 and Visit 3 TIA/stroke questionnaire data, age at Visit 3, gender, ethnicity, field center, blood pressure, anti-hypertensive medication, diabetic status, smoking status, total cholesterol and its fractions at Visit 1+ Visit 2 and Visit 3.

All Visit 3 participants, excluding those without retinal or stroke/TIA data. Demographic characteristics of the excluded will be compared to those of the included participants to illuminate any selection biases.