ARIC MANUSCRIPT PROPOSAL FORM

Manuscript #335

1. a. Title: Methods for evaluation of retinal microvascular abnormalities associated with hypertension/sclerosis: the ARIC Study
b. Abbreviated Title: Meth eval hyperten abnorm

2. Writing Group: Hubbard LD, Brothers RJ, Klein R, Davis MD, Cooper LS, Sharrett AR, Cai J

3. Timeline:

Analysis will begin with an interim set of data from all participants evaluated through mid Summer, 1995, for both generalized narrowing with image processor protocol and other signs with light box protocol, upon receipt from the Coordinating Center. Exploratory analyses will be conducted at at the Retinal Reading Center to construct algorithms for summarization of data from Retinal Reading Center, and to develop table shells for final paper. Analysis plan so developed will be implemented on final data set when available in early 1996.

4. Rationale:

Abnormalities of the retinal vasculature may reflect the degree of microvascular damage due to hypertension and/or sclerosis, which in turn may influence the type and severity of cardiovascular complications. Little is known about the relationships of these factors in modern, well-characterized populations. Nonmydriatic photogaphy provides a noninvasive and economical view of the retinal vasculature, which is being assessed according to standardized protocols.

In contrast to findings of epidemiologic studies carried out several decades ago, retinal vascular signs of longstanding hypertension are relatively infrequent in current populations with access to antihypertensive therapy. However, several of the focal signs evaluated by "traditional grading" (e.g., focal narrowing of arterioles, arterio-venous crossing changes, and hemorrhages/microaneurysms) are probably still frequent enough to contribute useful information.

Generalized arteriolar narrowing, perhaps the earliest retinal sign of hypertension, has previously been assessed imprecisely. Previous studies have developed a technique (based on that of Parr) which summarizes the caliber of all retinal arterioles emanating from the optic nervehead as a central retinal arteriolar equivalent (CRAE), which is scaled against a similarly estimated central retinal venous equivalent (CRVE). For ARIC, an computerized system has been utilized to enhance the image and measure the vessels. Lower CRAE/CRVE ratio (suggestive of narrowing) has already been shown to be stongly associated with higher blood pressure.

5. Main Hypothesis:

Various hypertensive/sclerotic abnormalities in the retinal vasculature (particularly generalized arteriolar narrowing, focal narrowing, and A/V crossing abnormalities) are associated with hypertension, controlling for confounding factors such as age, gender, race, diabetes, and anti-hypertensive treatment status, and can be evaluated with sufficient reliability. Although this paper is mainly descriptive, a staged classification of hypertensive/sclerotic abnormalities in combination (based chiefly upon generalized narrowing, focal narrowing of arterioles, and A/V crossing changes) may be constructed to see if it is more strongly associated

with hypertensive status than any single abnormality.

Association of retinal abnormalities with hypertensive status will be examined by comparing distributions of these signs across subgroups.

6. Data (variables, time frame, source, inclusions, exclusions):

Light box variables: focal narrowing on disc, focal narrowing zone A, focal narrowing of arterioles, sheathing of arterioles, A/V crossing changes, generalized narrowing, number of microaneurysms, number of retinal hemorrhages, type of retinal hemorrhage, hemorrhage/microaneurysms, hard exudate, soft exudate, IRMA, venous beading, macular edema, papillary swelling, proliferative DR, diabetic retinal level.

Image processor variables: CRAE, brance CRAE, CRVE, CRAE/CRVE, branch CRAE/CRVE, number of arterioles, number of venules, trunk/branch ratio.

Quality monitoring variables: variability of chief measures from light box and image processor protocols, expressed as intraclass correlation coefficients or kappa statistics as appropriate.

nonocular variables: age, sex, race, diabetes status, Visit 3 blood pressure and hypertension status (controlled/uncontrolled).

All Visit 3 participants, excluding those without retinal or BP data (demographic characteristics or the excluded should be compared to those of the included participants to illuminate any selection biases.