THE STRONG HEART STUDY
Cardiovascular Disease in American Indians
(Phase III)

Operations Manual
Volume Two
Personal Interview and General Examination

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For copies, please contact

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# VOLUME II
PERSONAL INTERVIEW AND GENERAL EXAMINATION

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Clinical Examination - General

1.1 INTRODUCTION

Tribal members who had resided in one of the study communities for at least 6 months and who were between 45 and 74 years of age during the examination phase were invited to participate in the Phase I physical examination. Persons who were institutionalized were excluded. All those who participated in the Phase I exam are eligible for the Phase II and III exams. This component of the study consists of a personal interview, a limited physical examination and laboratory tests. The objectives are to estimate the prevalence of CVD and its risk factors and to assess the degree of association between the risk factors and CVD.

The examination will be conducted at local IHS hospitals and clinics. In the Dakotas, it will be performed at the Aberdeen Area IHS hospitals and clinics on three reservations. In Phoenix, the Tribal hospital at Sacaton (GRIC), the Tribal outpatient clinic at Salt River (SRIC) and the outpatient clinical AkChin will be the examination sites. In Oklahoma, the IHS hospital in Lawton and the IHS clinic in Anadarko will provide space and facilities for the examination.

The objectives of the Strong Heart Study and the examination procedures will be explained to the participants and informed consent will be obtained from each participant. Appendix A-1 gives an example of the consent form which requires a signature by the participant.

All examinations are performed by trained personnel, nurse practitioners, registered nurses, medical students, physician assistants or physicians. All examination items are within the scope of training that these providers have received and are usual, if not daily, parts of physical examinations. Detailed descriptions and training are aimed at achieving consistency from examination to examination, and among centers. This is the main goal of this component of the protocol.

The training of the registered nurses, nurse practitioners, medical students, physician assistants and physicians on the Phase III protocol occurred on April 16-19, 1997 at the University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma and was based on the written protocol. Each Study Center has designated a primary examiner and at least one other person who is available to perform examinations in the absence of this primary person.

Certification requires adequate performance of the components of the examination as validated during training. In case of loss of a center's staff member, a replacement may be trained locally by someone certified in the procedure(s). The same certification requirements as used in the initial training must be met. Quality control focuses on the potential for false positive examinations. Because most participants are healthy, the frequency of abnormal findings is relatively small. The presence of real abnormalities among those with normal examinations is also small (a low false negative rate), and this makes it inefficient to re-examine the many individuals with normal findings. The review of positive findings is part of the medical data review. After the initial training, continuing education includes regular review of the protocol.
1.2 COMPONENTS OF THE CLINICAL EXAMINATION, ENDPOINTS AND RISK FACTORS

1.2.1 Components of the Clinical Examination

The clinical examination has two parts: a personal interview and a physical examination.

1. Personal Interview

The following questionnaires will be administered:

1) Demographic information: income, residence, marital status, number of household members and employment will be determined.

2) Health habits: Smoking, alcohol intake and the impact of gaming since casinos have been established in some communities will be assessed.

3) Medical history, including Rose questionnaire for angina pectoris and intermittent claudication will be assessed.

4) Dietary survey: The 24-hour recall instrument used with the National Health and Nutrition Survey and in Phase II of SHS will be re-administered following procedures utilized by NHANES.

5) Quality of Life: The Quality of Life instrument will be the same as in the Phase II using the Rand MOS SF 36 questionnaire.

2. Physical Examination

The physical examination includes the following procedures that were used previously:

1) Anthropometric measurements will be made with participants in loose clothing with shoes and heavy objects removed from pockets:

   i) Weight -- The scale will be balanced on a level and firm surface prior to weighing a participant. The participant will stand in the middle of the scale platform, head erect and looking straight ahead. Results will be rounded to the nearest kg.

   ii) Height -- The participant will stand erect on the floor with his back against the vertical mounted ruler, heels together and looking straight ahead. The right angle will be brought down snugly but not tightly on the top of the head so that height can be accurately measured and rounded to the nearest unit.

   iii) Waist and hip circumferences -- For the waist, anthropometric tape will be applied at the level of the navel with the patient supine and breathing quietly. Results will be rounded to the nearest cm. For the hip, the participant will stand erect but relaxed with weight distributed equally over both feet. The measure will be made at the level of maximum protrusion of the hips with the tape kept horizontal. These measurements are rounded to the nearest unit.
iv) Body fat measurement -- Using an RJL bioelectric impedance meter, resistance and reactance are recorded. Percent body fat will be estimated by the RJL formula based on total body water.

v) Arm circumference -- The participant will sit on a table so his right arm hangs freely with the right hand resting on the right knee. The tape measure will be placed horizontally at the midpoint between the acromion and olecranon. Results will be rounded to the nearest cm. The measure will be used to select the proper size blood pressure cuff.

2) Examination of the following:
   i) Pedal pulses -- The presence of posterior tibial (palpating inferior to the medial malleolus of each foot) and dorsalis pedal (palpating superior) pulses will be determined.
   ii) Ankle edema -- With foot coverings removed, participant will be examined in the supine position. Gentle but firm pressure will be applied along the mid-tibia, anteriorly down to the ankle in each leg. The degree of edema (0-4) will be recorded.

3) Blood pressure measurements:
   i) With the participant sitting with right arm on table, the cuff will be connected to a standard manometer and the pulse obliteration pressure will be established and recorded. After five minutes, the cuff will be reconnected and inflated to +30 mm above the obliteration pressure and held constant for 5 seconds. The cuff will be slowly deflated (2 mm/sec) while reading pressures for 1st and 5th phases. Before measurements 2 and 3 are taken, the participant will raise the arm for five seconds. After another 25 seconds with arm on the table, the measurement will be repeated a second and third time. The average of the last two measurements will be used for analysis.
   ii) Using a Doppler, with the participant supine, right brachial and both ankle systolic pressures will be measured two times.

4) Twelve-lead resting ECG measurement -- Using a Marquette Mac-PC-based system, a 12-lead EKG will be obtained in a standard manner. EKGS will be electronically transmitted to Cornell University and confirmed interpretations will be transmitted back to field location to be filed in the participant's medical record. Tracings will be Minnesota coded.

5) Glucose Tolerance Test (GTT) -- Fasting blood samples will be taken. Participants will be asked to drink 75 gm. glucose solution (Glutol) quickly (within 3 minutes). The participant will be instructed to take specimen container to the bathroom for urine sample. The second blood sample will be obtained at exactly 2 hours±3 minutes post-load. The GTT will be given to all participants, except:
   i) Insulin-requiring diabetic participants.
ii) Diabetic participants who are on oral agents and the previous record indicated at least two values of random blood glucose above 250 mg/dl, or fasting glucose 225 mg/dl. on the day of the exam by One Touch glucometer.

iii) Non-diabetic participants with a fasting glucose of 225 mg/dl. or higher by One Touch glucometer.

6) Fasting blood samples for measurements of total triglyceride (TG) and cholesterol, LDL and HDL cholesterol, plasma fibrinogen, and PAI-1, and DNA isolation, glucose, creatinine, insulin, and SMA-12 will be obtained. Only tubes for DNA will be taken from patients who are on renal dialysis or have had a kidney transplant.

7) Urine will be collected at the beginning of the physical examination for measurement of albumin and creatinine.

8) Peripheral sensation will be measured in the right foot by monofilaments. Both feet will be examined for possible ulcers.

9) The following procedures will be added:

i) **Echocardiography of the carotid artery:** See Volume VI of the Manual for details.

ii) **Carbon monoxide in exhaled air** will be measured to validate smoking status.

At the beginning of the examination, after fasting blood specimens are obtained, the participants will be asked to take a breath and exhale forcefully into a Vitalograph "BreathCO" meter. The digital reading of CO in ppm is instantaneous. The participants will be asked when their last cigarette was smoked and how many cigarettes were smoked in the last 24 hours. History of exposure to smoke in the environment will also be obtained. CO readings in the range 15 to 50 ppm are most often seen in smokers, readings in the range of 9 to 14 ppm are usually seen with environmental tobacco smoke exposure and readings 0-8 ppm are usually seen in persons who have not been exposed to smoke for 24 hours. The results will be interpreted immediately to the participants who smoke or who are exposed to smoke and they will be advised to quit or cut down on smoking and/or establish a smoke-free environment in their houses or workplaces.

High readings in persons not exposed to smoke will be referred to IHS Environmental Health Program for follow-up evaluation for faulty heater or vehicle exhausts.

iii) **Ambulatory pulmonary function (PF) monitoring** -- A hybrid nested case-control/cross-sectional design for the study of asthma will include as "cases" all those who reported asthma or asthma symptoms during the Phase II examination, along with an age, gender and tribe-matched control group of
healthy non-smoking participants without respiratory symptoms or cardiopulmonary disease. Approximately 600 cases will be identified and about 200 of controls will be selected. Cases and controls will be asked to perform peak expiratory flow (PEF) measurements using a hand-held battery powered electronic spirometer that can store results for two weeks of testing, eliminating the need for written daily. The participants (cases and controls) will be asked to measure PEF at least twice a day for two weeks. An addressed, stamped, and padded envelope will be provided so that the participants can return the spirometer after two weeks of monitoring. This will be performed using methodology comparable to the Cardiovascular Health Study.

The IHS medical records will also be reviewed to determine whether the participant was hospitalized or received out-patient treatment for ESRD, stroke, myocardial infarction, or other manifestation of CVD since the previous Strong Heart Study examination.

A checklist to be used for the physical examination and a reminder of post examination activities are given in Appendix A-2 (a) and (b).

The clinical examination will last approximately three hours. The participant will arrive at the clinic fasting in the morning. After registration, a study staff member will explain the study and procedures to the participant, answer questions, if any, and have the consent form signed. The participant will then be instructed to go to the laboratory for blood drawing, to drink the glucose preparation (Glutol), and to obtain the urine specimen. The nurse clinician and other staff will then conduct the personal interview, examination of the lungs, obtain anthropometric measurements, blood pressure, impedance measurement for body fat composition, and ECG measurements. At exactly two hours after the ingestion of the glucose preparation, the participant will have another blood sample drawn for the glucose tolerance test. If the above procedures are not completed before the 2-hour sample is drawn, they may be continued and completed after the participant consumes a light snack. After all the procedures are completed, the participant will receive the payment or sign the payment form and be thanked for his/her participation.

If possible, all of the components, except for the dietary survey and echo exams, should be completed in one visit. If an individual leaves before the examination is completed, it must be completed before the study is completed. The personal interview and consent may be completed up to two weeks prior to the physical examination if such arrangements are more convenient.

1.2.2 Components of the Examination for Family Members

The family members will have all the information collected that is described above for the Phase III exam of the cohort, except for the ambulatory PF monitoring. Each center will pilot the family member exam in at least 10 persons and appropriate revisions in the procedure will be made and standardized for use in all three centers for 300 family members age 18 or over at each center. For pregnant women, the examination will be conducted no earlier than six weeks after delivery. Lactating women will be included in the study if sex weeks or more postpartum. As much of the information as
possible that was collected on the original participants will be collected on the family members. The interview will include the following:

i. Phase II Information: This includes: tribal enrollment, degree of Indian blood, marital status, education/income, use of native language, smoking and alcohol use, medical conditions, reproductive history, and current physical activity.

ii. Phase II Information includes: history of attending boarding school, respiratory/snoring, cultural factors, risk factor knowledge, quality of life.

1.2.3 Endpoints and Risk Factors

A. MORBIDITY EVENT CRITERIA

1. Definite Myocardial Infarction (MI)

Minnesota codes 1.1.x or 1.2.x except 1.26. and 1.28 with no 7.1 or 7.4
History of MI verified by chart review as definite MI

2. Possible Myocardial Infarction

Minnesota codes 1.3.x, 1.2.6, or 1.2.8 with no 7.1 or 7.4
History of MI verified by chart review as possible MI

3. Definite Coronary Heart Disease (CHD)

Definite MI,
Definite CHD verified by chart review to include cardiac cath, proven coronary artery disease, PTCA, coronary artery bypass grafting, or abnormal stress ECG plus abnormal imaging (i.e., both must be abnormal),
Angina Pectoris plus LBBB (7.1.1) or
ST changes (4.1) or
T wave changes (5.1) or
verified possible MI,

4. Possible Coronary Heart Disease

Possible ECG MI (1.3.x, 1.2.6, 1.2.8)
Angina Pectoris
Minnesota codes 7.1, 4.1, 4.2, 5.1, 5.2, 7.4
Unconfirmed history of MI
Positive functional test of ischemia (such as treadmill) without invasive confirmation
Possible ECG or imaging in scintigraphic studies (not both).
5. **Definite Cardiovascular Disease (CVD)**

- Definite CHD
- Congestive Heart Failure
- Cardiomyopathy
- Valvular Heart Disease
- Left ventricular Hypertrophy by Echocardiogram
- Left ventricular Hypertrophy by ECG (3.1 or 3.3 plus 4.1-4.3 or 5.1-5.3)
- Ankle Arm Index \( \leq 0.8 \)
- Atrial Fibrillation
- Minnesota codes 4.1, 5.1, 6.1, 6.2, 6.8, 7.1, 7.2, 7.4
- Non-coronary heart surgery or carotid or other vascular surgery
- Pacemaker implantation
- Bruits by physical examination
- Intermittent Claudication by Rose Questionnaire
- Positive non-coronary angiography

### 1.3 RECRUITING

#### 1.3.1 Recruitment Techniques

Recommendations from the Dakotas’ Lillian Brown

**Always** remember that the participant is here on a **voluntary** basis.

Recruiting participants to the Strong Heart Study is more than simply getting the person to come into the clinic for an exam. Their participation in the Study is the result of an ongoing effort of Strong Heart personnel to recognize, establish trust with, and care about the people who take time to participate in the Study. Without our participants, we have no Strong Heart Study.

Greet people wherever you see them. Call them by name and make the effort to greet them first.

Take time to be in places like the Tribal Office, Post Office, Hospital and any location where there is a large gathering of people. Talk gently with them about other subjects and then slowly talk with them about Strong Heart participation.

Don’t sit in the car and honk the horn when making home visits. Walk to the door and tell them why you are there. Take the initiative to visit with them first and see how they are.

People without a car often feel shut-in and frustrated. It is important to visit with them about a variety of things first before approaching them about participating in the Study.

Sometimes, when possible, it helps to offer a helping hand in things that need to be done, let people know that you recognize them as a person and not only a participant.
Dress casual and never act like you can’t be touched with a ten-foot pole.

Enjoy your home visits as most people like someone coming in with a smile. It really helps to enjoy what you do.

Be patient and explain things in a variety of ways so that people will understand what they are being asked to do.

**PLEASE,** always remember that the client is a volunteer. Treat them with courtesy and recognize that they have often gone to a great deal of effort in both time and energy in coming into the clinic to participate.

Recruiting is not a 9 to 5 job. It is important to recognize the people who do it very well and to support them.

Set goals that are clear to all personnel and allow sufficient time for the recruiters to reach them. Everyone should contribute to the recruitment effort.

Recognize the circadian rhythms of your community. Some participants are affected more by the community events, seasons and check days than others are. Try to be sensitive to the participants needs when scheduling.

Be willing to let the participant take part in as much as possible. Although it is ideal to have the participant complete the entire exam at once, it is not always possible. Be willing to adjust your schedule to accommodate the participant.

Regular team meetings are important in setting goals, communicating with team members in a meaningful way, in helping to focus efforts and in supporting the efforts of the personnel. Sometimes personnel can become discouraged when events do not go like they were planned. This does not have to mean that things are going badly. Be aware of staff burn-out and the need to stop and to promote other team members or to give them a helping hand.

1.3.2

All individuals who participated in the Phase I exam are eligible for the Phase III clinical examination. Eligible study participants are identified through the Strong Heart Study data base. Individuals will be contacted in an order convenient for each center. Local publicity campaigns and mailed information will alert participants before participation is requested.

When contacting an eligible participant, the interviewer introduces the Strong Heart Study and explains its purpose and importance. A brochure and a letter explaining the purpose of the study and exam are used for recruitment. The voluntary nature of the study and the confidentiality of the collected data are stressed. If the subject is not at home at the time of the phone call or visit, call backs are made as necessary to meet the individual and schedule the clinic appointment. 100% participation is the goal.
In all areas, the recruiter should wear an identification badge. When scheduling appointments the recruiter should emphasize the following:

1. That the volunteer should not eat breakfast the morning of the visit to the exam; and should not eat or drink anything but water after 9:00 p.m. the previous evening.

2. That the volunteer should bring with him/her all medications which he/she has been prescribed and is currently taking;

3. That the volunteer should not take their morning diabetes medication until blood drawing is completed;

4. No tobacco or vigorous activity before the clinic visit;

5. Volunteer should be instructed to wear loose clothing and ladies to wear a skirt and blouse or pants and shirt, rather than a dress

If the participant is related retarded or otherwise mentally incapacitated, a surrogate must accompany him/her to the examination, preferably someone who is very familiar with the medical and family history.

The recruiter schedules the appointment with the clinic for each subject. Whenever possible, eligible members of a single household are scheduled on the same day. The recruiter should also verify name, address, and social security number at the time of the recruiting visit. When possible, participants should be reminded by phone or in person the day prior to the visit.

After the visit appointment is made, the clinic staff should assemble all forms and labels necessary for the exam and arrange to have the hospital chart for that participant available the morning of the clinic visit. The chart may also be reviewed to see if the participant satisfies the exclusion criteria for the glucose tolerance test.

1.4 PERSONAL INTERVIEW

1.4.1 Components of the Personal Interview

The personal interview is designed to obtain demographic information, medical history, health behavior, acculturation and stress data that are considered important in identifying risk factors for cardiovascular disease. The following questionnaires will be administered during the clinical examination:

1. Personal Interview Form (I and II)
2. Gambling
3. Medical History Form
4. Dietary Form
5. Sleep Habit
6. Quality of Life
7. Respiratory (family study members)
8. Physical Activity (family study members)

Personal living habits such as dietary, cigarette smoking and alcohol consumption, and stress have been considered as important risk factors for cardiovascular disease. Data on these factors as well as demographic information and the degree of acculturation will be collected by using the Personal Interview Forms (I and II). Medical History Form which consists of questions on medical conditions, medications used and the Rose Questionnaire for angina pectoris and intermittent claudication. These questionnaires are given in Appendix C.

1.4.2 Guidelines for Interviewers

1. Introduction

The personal interview is probably one of the most important procedures for data collection in epidemiologic research. The personal interview has been shown to increase response over self-administered questionnaires. When rapport is established between the interviewer and the interviewee it has been shown to be an excellent source of high quality information for epidemiologic research purposes. However, the interviewer must be able to show tact, care, and sensitivity, to be effective. Not everyone can become a successful interviewer.

Also, the personal interview can lead to a lack of standardization in the data collected, particularly in a multi-center study such as the Strong Heart Study. Since the interviewer is known to have a large effect on the quality of the data obtained, therefore interviewer training is very important. Please read this interviewer's manual frequently, and refer to it as needed during the study. It is also recommended that each Study Coordinator, hold monthly interviewer meetings, to go over common problems and clear up any questions about the interview procedures and the interview forms in the Strong Heart Study.

2. Types of Interviews

Structured versus Unstructured Interviews

In an unstructured interview the responses to questions are open-ended, and information given is to be recorded as given. In a structured interview the questions are usually closed, with a specific set of answers provided in the questionnaire.

For the Strong Heart Study we are using both structured and unstructured interviews. The use of structured interviews is the best way to maintain consistency in the data being collected. Interviewer training is important in order to maintain as much consistency in the interviews between study centers as possible.
Because we are using structured and unstructured interviews, we can achieve even more consistency if all interviewers conduct the interviews in a similar way. Therefore, ask each question as it is written. Do not reword the question. Also, ask the questions in the order they are given in the interview form. Hopefully, by following these procedures we can achieve a high degree of consistency in the way the interviews are conducted.

3. **Style of the Interview**

The interview style is also important and some of the components that are generally considered to be acceptable interview style are listed below. In addition to the components of style listed below, the following interviewer characteristics are also very important: Politeness is very important since we will be asking sensitive questions to strangers, in a situation where they may be uncomfortable. Sensitivity on the part of the interviewer is also important, in order to know how and when to be more or less assertive in asking for information. Besides these qualities, please develop your style in accordance with these guidelines:

a. **Non-judgmental, non-evaluative style.** A large portion of the impression which the respondent has of the interviewer is based solely on the interviewer's voice and the manner with which the interviewer responds to the respondent's comments. A judgmental or evaluative response would indicate that the interviewer has made a judgement of the relative goodness, appropriateness, effectiveness, or rightness of the respondent's statement. The interviewer should not, in response to the respondent's statements, state what the respondent should or should not do in a given situation. The interviewers task is simply to record the information provided, and to elicit the desired response.

b. **Non-interpretive style.** As above, the interviewer should not use a style that might be considered teaching or preaching. An interpretive response is one which indicates that the interviewer's intent is to teach. We are interested in the respondent's impression of what was happening, not in the interviewer's impression.

c. **Allow for respondent to complete sentences.** Do not try to help the respondent by answering the questions for him/her. No matter how slowly the respondent is speaking, putting words in the respondent's mouth or not allowing the respondent to finish thoughts will generally alter the information which the respondent is attempting to give. However, long hesitations may be bridged by asking appropriate questions.

d. **Supportive remarks.** Remarks which indicate that the intent of the interviewer is to reassure, to pacify, or to reduce the intensity of the respondent's feelings are appropriate. However, these should be in keeping with local terms and expressions, and should be short so as not to detract from the interview itself.

e. **Probing.** This is an important response style which will be discussed further. A probe is a response which indicates that the interviewer's intent is to seek further information, to
provoke further discussion along a certain line, or to question the respondent. Direct
probes will be specific questions about details of what the respondent said.

f. Non-directive, or understanding. A typical non-directive response might be "I see". This is the general idea of understanding murmuring or clucking. The interviewer might also repeat what the respondent just said. This may prompt the respondent to elaborate.

4. Gain Rapport with the Interviewee before Commencing Interview

The first step in gaining the confidence of the respondent is a straightforward, believable introduction of the interview and the reason for this contact. It may help in gaining rapport with the respondent if you tell him/her a little about yourself, such as where you are from, and your background, etc. If the respondent seems to hesitate or has some questions the interviewer must be prepared with a more detailed explanation of why the information is needed. Also, if the respondent raises the issue of the confidentiality of the information collected, the interviewer must be prepared to reassure him/her of the precautions taken to respect their privacy.

5. Interviewer Error

We should try to minimize interviewer error during this study. The primary objectives of epidemiologic research are (1) to obtain measurements of exposure and disease variables relevant to the objectives of the study, and (2) to minimize error in these measurements. The presence of an interviewer may both reduce error and increase error. It may reduce error by increasing the response rate, motivating the subject to respond well and probing to obtain complete data when the responses volunteered fall short of what is desired. The presence of an interviewer may increase error if by his or her appearance, manner, method of administration of the questionnaire or method of recording of the responses he or she exerts a qualitative influence on the subject's responses. Possible sources of error in the interview for data collection include (1) conditions of administration (heat, light, ventilation, freedom from distraction, lack of time, etc.); (2) interaction of the personality (sex or race of the interviewer with that of the subject); and, (3) performance by the interviewer (questioning, prompting and recording of responses).

The following are the common interviewer errors:

a. Asking errors. Omitting questions or changing the wording of questions.

b. Probing errors. Failing to probe when necessary, biased probing, irrelevant probing, inadequate probing, preventing the respondent from saying all he or she wishes to say.

c. Recording errors. Recording something not said, not recording something said, incorrectly recording response.

d. Flagrant cheating. Not asking a question but recording a response, recording a response when the respondent does not answer the question asked. These kinds of errors do occur.
and this has been amply documented by various studies. Cheating has been shown to be more common when the interviewer is in an uncomfortable situation with the interviewee, i.e., he/she is difficult. In such situations the question should still be asked and if the participant refuses to answer the question(s), the refusal should be documented on the form.

6. Circumstances for the Interview

We will not have very much control over the circumstances for the interviews. However the following should be considered in arranging for conducting interviews:

a. Time. There will be little control over the time of the interviews, since we will have many different interviews to carry out over a short period of time. When possible, the interview should be conducted after the snack has been served, otherwise the interviewee may tend to be somewhat uncomfortable.

b. Place. The place for the interview should be chosen where there are as few distractions as possible. Try to select a place where the location is quiet and comfortable. If it is possible, it is ideal to sit at a table, with the interviewer facing the interviewee, so that the interviewer can organize the papers. Privacy is also important. If the respondent will need to refer to records during the interview, be sure that the records are available before the interview begins.

7. Asking Procedures

In general the rules for asking questions in structured interviews can be summarized as follows:

a. Questions must be asked according to the instructions for each form. Be sure to read and re-read the instructions for each questionnaire you are using, and to ask all the questions in the same way to each person interviewed.

b. Read the questions exactly as they are worded in the questionnaire. If the question is misunderstood, then it may be repeated, interchanging local terms, if necessary for understanding.

c. Read each question slowly.

d. Use correct intonation and emphasis.

e. Ask the questions in the order that they are presented in the questionnaire.

f. Ask every question that applies to the respondent (all inapplicable questions will be identified as such by skip instructions in the questionnaire).
g. Repeat questions IN FULL that are misheard or misunderstood.

h. Read all linking or transitional statements exactly as they are printed.

i. Do not add apologies or explanations for questions unless they are printed in the questionnaire.

**PROBING:** Probes are additional questions asked or statements made by the interviewer when the answer given by a respondent is incomplete or irrelevant. Probing has two major functions: (1) To motivate the respondent to reply more fully; (2) to help the respondent focus on the specific content of the question. It must fulfill these functions without biasing the respondent's answers. However, probes, when they are used, MUST be neutral. Probing can introduce bias, such as by summarizing your understanding of the response to the subject when an unclear response has been given, or by offering some alternative interpretations from which the respondent can choose, and this must be guarded against.

The following are NON-DIRECTIVE methods of probing:

a. Repeat the question (RQ). All that may be required to clear up a vague answer may be to repeat the question. You may begin by saying "I am not sure that I understood you, let me just repeat the question so that I can be sure to get your answer right."

b. The expectant pause. Waiting expectantly will tell the respondent that the interviewer is expecting more information than has been provided.

c. Repeat the reply. Repeating the reply aloud while recording it may stimulate the respondent to provide more details.

d. Neutral questions or comments. Various neutral probes may be used for purposes such as clarification, specificity, or completeness: "What do you mean exactly?", "In what way?", "Could you be more specific about that?", "Anything else?", "Can you tell me more about it?"

e. Interpretation. Make sure that the question was understood, since that may be the reason for incomplete answers. You may need to ask the question again, perhaps substituting some local terms, if there is a problem in interpretation.

**FEEDBACK:** The provision of feedback by the interviewer to the respondent about his or her performance has been the subject of much research. Some studies have shown that the use of feedback in health-related surveys increased the amount of reporting of most events. Your decision about whether to provide feedback may depend upon the performance of the person you are interviewing, and your experience in the benefits of providing feedback.

8. Specific Instructions for Telephone Interviewing
While it is generally held that the principles outlined above, which have been derived solely from research into and experience of face-to-face interviewing, apply to telephone interviewing, the evidence that this is true is very limited. Telephone interviewing is probably not simply the transfer of face-to-face techniques to the telephone. Use of visual cues, such as "show cards", is impossible on the telephone and must be compensated for in questionnaire design. There is evidence that this compensation may lead to response differences. In addition, other non-verbal communication, both from the interviewer to respondent and respondent to interviewer, is absent. The "expectant pause", for example, may be much more difficult to use as a probe for additional information on the telephone. It is also more difficult for the interviewer to establish the legitimacy of the interview on the telephone and the pace of the interview may be faster (because of the need to keep talking) leading to hurried and, perhaps, less thoughtful responses. On the positive side, the telephone should eliminate non-verbal biasing activity by the interviewer, and may encourage more honest reporting of threatening behaviors. Empirical data, however, have not shown consistent evidence of these effects.

9. Instructions for Recording Responses

In the study manual, each interview and form contains a set of question by question instructions for filling out the interview form, to clearly describe the information that is being solicited. These instructions should be read carefully and understood before attempting to fill out an interview form.

In addition, see the attached instructions for filling out forms. The following are some additional guidelines for recording responses:

a. Make sure that you understand each response.

b. Make sure that the response is adequate.

c. Do not answer for the respondent (i.e., do not infer a response from an incomplete or inadequate reply).

d. Begin writing as soon as the respondent begins talking. (The respondent's interest may be held by repeating the response aloud as you are writing).

e. Use the respondent's own words and record the answers verbatim.

f. Include everything that pertains to the question's objectives.

g. Note in the questionnaire the nature and place of each probe used.

h. Do not erase anything. If a response is wrong, strike it out and enter the correct response.

i. Write "refused" beside any question that the respondent refused to answer.
1.4.3 Training & Quality Control of Interviewers

1. Training

Interviewers were centrally trained in April 1997 at the training session in Oklahoma using a standardized procedure for administering each questionnaire. Training included instructions in research interviewing techniques and in completing each form. Interviewer skill training included:

(a) adherence to the standardized protocol  
(b) use of non-judgmental attitudes  
(c) degree and nature of prompting permitted  
(d) dealing with problem interviewing situations  
(e) handling participants’ comments and recording relevant information on the note logs  
(f) post-interview responsibility for the data

2. Quality control of interviewers

To insure consistency and accuracy and to minimize inter- and intra-interviewer differences, study coordinators will monitor 5% of the interviews done by each interviewer.

1.5 RATIONALE FOR MEASUREMENTS

1.5.1 Blood Pressure

As blood pressure rises, so does risk of ischemic heart disease and its complications. The range of normal blood pressures is wide. Even within the "normal range", risk increases as the upper limits are approached. Usually, blood pressures are expressed as systolic pressure/diastolic pressure; values 140/90 mmHg or higher are considered to be hypertensive for adults. Middle-aged persons with a diastolic blood pressure of 90-104 mmHg (so called "mild" hypertension) have a risk of heart attack that is about 70 percent higher than that of persons with a diastolic pressure under 80 mmHg (normal value). Persons with a diastolic blood pressure exceeding 104 mmHG (moderately severe to severe hypertension) have a risk more than twice that of those with a normal value. Hypertension is an especially strong risk factor for stroke and, to a lesser extent, for peripheral vascular disease. Most of the knowledge of the consequences of high blood pressure arises from studies of sitting arm blood pressure.

1.5.2 Measurement of Body Fat

Population studies have always demonstrated a uni- variate association between obesity and CVD. However, in many early studies, the association between obesity and the incidence of CVD did not remain significant in multi-variate analysis, and thus it was thought that obesity was a risk factor solely because of its influence on other risk factors such as blood pressure, plasma lipoproteins and diabetes. More recently, especially in longer term studies, significant independent associations between obesity and the incidence of CVD have been demonstrated.
Although early records are not conclusive, all evidence indicates that obesity among American Indians was rare until the last century. Their farming and hunting life styles which were associated with high degrees of physical activity and the lack of consistently abundant food sources, probably assured the maintenance of a lean population. However, with the advent of "Westernization" and the reservation system, obesity has increased steadily among all Indian tribes and is now a major health problem. It is thus essential to evaluate the extent of obesity in the individuals in this study in order to ascertain its role in cardiovascular disease as well as its relationship to risk factors such as diabetes and hypertension.

In the past, assessment of obesity in population studies was invariably accomplished either by algorithms such as ratios of weight to height, or by measurements of skin folds using calipers. This was because assessment of body composition required either very expensive equipment or time consuming procedures, such as underwater weighing. Within the past few years, instrumentation has become available to allow estimates of body composition from measurements of tetrapolar impedance. This measurement of bioelectrical impedance is quick and easy to perform and has been extensively validated against densitometry. These validations were first performed by Lukaski et. al. and by Roche et. al., in a wide variety of individuals. The conductivity increases in individuals with low percent body fat and the instrumentation calculates the percent body fat utilizing a computerized algorithm.

1.5.3 Anthropometric Measurements

It has been recently demonstrated that among obese individuals, the distribution of body fat is related to certain patterns of morbidity. Vague and co-workers have observed that body fat distribution differs among obese individuals, and that obese subjects can be roughly divided into two groups depending on whether accumulation of body fat is subcutaneous and peripheral (referred to as gynecoid or female type obesity) or whether the fat accumulation is central and primarily in the omentum (referred to as central or android obesity). The latter distribution has been shown in a number of studies to be consistently associated with the triad of hypertension, insulin resistance, and cardiovascular disease. Most studies have shown that central obesity is a risk factor for coronary artery disease.

No systematic studies of body fat distribution have been made among the American Indians. However, visual observations suggest that central obesity is much more prevalent among this racial group.

The quantification of central vs. peripheral obesity is not well standardized. Original studies were done simply by photographs and visual evaluations. This was supplanted by body circumference measurements with investigators generally taking the ratio of the body circumference at the waist to the hip or the thigh as a measure of fat distribution. However, it is clear that the body fat of interest in central obesity is the non-subcutaneous, and therefore, whole body scanning devices are necessary for a precise evaluation of this depot. Nevertheless, it has been shown in a number of population studies that the comparative circumference measurements are an approximation of the body fat distribution and the only practical techniques usable in a field study.
1.5.4 Measurements of Peripheral Vascular Disease

The atherosclerotic process affects vessels in many parts of the body. While the most conspicuous morbidity and mortality arise from coronary atherosclerosis, large vessel peripheral arterial disease (PAD) often results in significant incapacitation of the lower extremities and has been also strongly associated with the incidence of coronary heart disease. Criqui and co-workers have shown that large vessel PAD is strongly and significantly predictive of all cause mortality in both sexes with a relative risk of 4 to 5, and this was independent of other cardiovascular risk factors in a multi-variate analysis. Moreover, data from the Framingham study indicate that diabetes was associated with an even greater magnitude of increase of peripheral vascular disease than was coronary heart disease.

A thorough evaluation of peripheral arterial occlusive disease usually entails both a history and a physical examination including measurements of pulses and segmental blood pressures and then more complex measures such as angiography or sonography. The latter two techniques are both expensive and difficult to apply in a field setting. On the other hand, both Criqui et al and Beach et al have used segmental blood pressures measured by a simple doppler instrument in studies involving hundreds of patients. In addition, the correlation between quantitative velocity measurements and segmental blood pressures with occlusion as measured directly by angiography has been established.

Because of time limitations and economic consideration for purchase of equipment, the following indices of peripheral vascular disease will be made in this study.

1. Rose Questionnaire for intermittent claudication.
2. Palpation of posterior tibial and dorsalis pedis pulses.
3. Measurement of the ratio between blood pressures taken at the antecubital fossa (brachial) and ankle (posterior tibial) using a doppler listening device (Imex Mascot Model).

1.5.5 Electrocardiograms

All participants will have a resting electrocardiogram so that evidence for ischemic changes and left ventricular hypertrophy can be determined. The prevalence of such changes will reflect the prevalence in the population studied and can be compared to other population-based studies and among the three sites.
1.5.6. Overview of Laboratory Measurements

1. Lipoprotein Profile

Lipoprotein Physiology: Lipoproteins are basically spherical particles ranging widely in size and composed of two components: the lipids (or fats) in the core of the particle and the proteins on the surface of the particle. The two types of lipids which we are interested in measuring as part of the present research are triglyceride (TG) and cholesterol (CHOL). Depending on the relative amount of these two components and various associated proteins, different classes of lipoproteins can be defined (Table 1.1).

<table>
<thead>
<tr>
<th>Class</th>
<th>%Lipid</th>
<th>% Protein</th>
<th>Origin and Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chylomicrons</td>
<td>99</td>
<td>1</td>
<td>Intestine; transport of newly absorbed dietary fats; normally not detectable in plasma after a 12-hr fast; creamy layer on top of plasma tube after 12 hrs in the refrigerator.</td>
</tr>
<tr>
<td>VLDL, very</td>
<td>90</td>
<td>10</td>
<td>Liver; transport of newly synthesized triglycerides to peripheral tissue; lipoprotein approximately 80% of plasma TG is in this fraction</td>
</tr>
<tr>
<td>low density</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL, low</td>
<td>75</td>
<td>25</td>
<td>Liver; derived from VLDL after the have been metabolized; transport of cholesterol; approximately 75% of plasma cholesterol is in this fraction</td>
</tr>
<tr>
<td>triglycerides</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>density</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>lipoproteins</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL, high</td>
<td>45</td>
<td>55</td>
<td>Liver and intestine transport of cholesterol from peripheral tissues back to the liver</td>
</tr>
<tr>
<td>density lipoproteins</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The evidence is overwhelming from both cross-sectional and prospective studies in a wide variety of populations that total and LDL cholesterol are significantly associated with the occurrence of
atherosclerotic coronary vascular disease (ASCVD), and the HDL cholesterol has a negative or "protective" effect.

The relationship with total triglycerides or VLDL triglycerides has been more controversial. Several population studies have now demonstrated an independent positive association between elevated triglycerides and ASCVD. Triglycerides are also closely linked to obesity, hyperglycemia and low HDL, and are therefore important to measure because of their reflection of these disorders. Some of the ambiguity concerning the associations between triglycerides and coronary vascular disease stems from the possibility that all elevations in triglycerides may not be equal. That is, elevated VLDL with a high proportion of protein, or cholesterol rich VLDL such as that observed in many diabetics may be more atherogenic than large, triglyceride-rich VLDL.

If a Beta Estimate is performed, measurements are made of total plasma cholesterol and triglyceride. HDL is measured after precipitation of LDL and VLDL. LDL is calculated by the Friedewald formula:

\[ \text{LDL chol} = \text{Total Chol} - \text{HDL Chol} - (\text{Total TG}/5) \]

This estimate is based on the assumptions that VLDL cholesterol is a minor portion of the total cholesterol, that the majority of the total triglyceride is in VLDL, and that the composition of the VLDL is "normal", that is, VLDL cholesterol is approximately one fifth that of triglyceride.

This method has two advantages:

1. Can be performed on plasma that was frozen.
2. Requires much less technician time.

The disadvantages are:

1. It is inaccurate in individuals with high triglycerides (> 400).
2. It is inaccurate in individuals with altered VLDL composition.
3. It will not allow the isolation and examination of VLDL composition and relations to ASCVD.

If Beta quantitation is performed, total cholesterol and triglyceride are measured, and HDL cholesterol is measured after precipitation, as in the beta estimate. In addition, VLDL is isolated by ultracentrifugation, and the ratio of cholesterol to triglyceride is measured in VLDL. From this we can directly calculate:

- LDL-Chol = Bottom-chol - HDL-CHOL
- VLDL-Chol = Total chol - Bottom chol
- VLDL-Triglyceride = VLDL-Chol x [VLDL-TG/VLDL-Chol]

The advantages are:
(1) LDL cholesterol is measured directly, not estimated.
(2) A measure of VLDL composition is obtained.
(3) VLDL and bottom fractions are available for further apoprotein measurements or for storage.

The disadvantages are:

(1) The ultracentrifugation is laborious, time consuming and costly.

The Beta quantitation procedure is selected because of the need for accuracy in the measurement of LDL and because it yields a VLDL fraction of particular interest in a population with high prevalence of diabetes. People with diabetes frequently have abnormal composition of VLDL.

2. Glucose Tolerance Test (Glucose and Insulin)

Although it may be argued that 75 gm glucose load is not a measure of glucose disposal that is analogous to carbohydrate ingested during daily meals, it is the standard measure of glucose tolerance which can be compared to other studies, and forms the basis for all the currently used criteria for diagnosis of diabetes. Because of the high prevalence of diabetes in all three centers, and because of the multiple previous studies reporting associations between diabetes and CVD, a glucose tolerance test is essential for the current study. The most simple to perform is one where blood samples are drawn by venipuncture at fasting, and then two hours after ingestion of the glucose. All other fasting blood samples may be obtained at the time of the fasting sample, thus limiting the venipunctures to two.

Glucose concentrations will be measured in both fasting and two hour samples. Blood for this is obtained in tubes containing fluoride to prevent consumption of glucose by WBCs. Previous studies in Phoenix have shown that tubes of blood containing fluoride can be held on ice for up to four hours before isolating the plasma, and glucose values are stable. Glucose is measured on the Hitachi analyzer using a glucose oxidase technique.

3. Insulin

Insulin concentration in blood has been reported in several recent studies to be an independent risk factor for the development of CVD. Although the mechanism of this association has not been established, there are several intriguing possibilities involving its link with insulin resistance, hypertension, hypertriglyceridemia, and thrombosis. The first three factors have been linked in several population studies in individuals with central obesity. However, some studies suggest that these factors are not universally associated. It will thus be of interest to measure fasting insulin concentrations in individuals at the three centers, to evaluate its relationship to vascular disease and also to blood pressure, triglycerides, waist/hip ratio and fibrinogen.
Insulin will be measured using an overnight radioimmunoassay developed as a modification of the method of Morgan and Lazarow. It utilizes a double antibody method; both antibodies and labeled insulin can be obtained efficiently from commercial sources. Although no absolute reference plasma pools are available for insulin, we have constructed our own control pools. The assay has proven to be stable over time with a coefficient of variation of 8-10%. One source of error in insulin measurements occurs in some individuals who have been previously treated with insulin, and thus have circulating insulin antibodies. Samples from insulin treated diabetics will be flagged at the time of drawing, so that their data can be separately evaluated.

4. Fibrinogen

Disorders of the coagulation system could play a major role in ASCVD. There has been special interest in the role that abnormalities in the clotting system might play in the increased risk for atherosclerosis observed in diabetics. Abnormalities in several factors have been reported to be associated with atherosclerosis. One of the most commonly and easily studied is fibrinogen, and it has been shown to be an independent risk factor for CVD in both nondiabetics and diabetics in the Framingham study.

Fibrinogen has been most commonly measured using a chromometric technique. For this, thrombin is added to plasma to induce clotting, and the clot is quantitated on a fibrometer or automated coagulometer. Since the lab at the MRI does not possess this equipment, measurements will be made by Dr. Russell Tracy at the University of Vermont.

5. DNA

Because CVD is a clinically heterogeneous disorder and involves a complex interaction between genetic and environmental factors, it will probably be explained by a complex polygenic transmission. Recent development in recombinant DNA technology, including using restriction enzymes to identify polymorphisms, are now frequently being used in the study of genetic disorders and may be very helpful in sorting out the genetics of complex diseases such as atherosclerosis. Methods are now available for detecting altered nucleotide sequence in the human genome, which may be used as genetic markers of CVD or risk factors. Certain alterations in DNA sequence may be demonstrated by cleaving genomic DNA with restriction enzymes, hybridizing with cloned DNA probes and by detecting changes in the length of gene fragments by autoradiography. These techniques have allowed the chromosomal mapping of the genes for diseases such as muscular dystrophy and Huntington's chorea.

Although we do not yet have evidence in Indians that CVD shows familial aggregation, there is certainly ample indication in other populations that CVD and several of its risk factors are familial and thus would lend themselves to genetic studies. Although genes for cardiovascular disease have been localized in animals, attention in human studies has been focused on identifying alleles that may be associated or linked with other diseases. Since diabetes, hypertension and altered lipoprotein concentrations are strong risk factors for the development of CVD, attention has been focused on the possibility that abnormalities in
apoprotein or insulin gene loci might be associated with susceptibility to CVD. Mandrup-Poulsen et al. have suggested that a polymorphic region of DNA close to the human insulin gene is a genetic marker for atherosclerosis. Karathanasis et al. have shown that the genes for Apo-A-I and apoC-III are physically linked, and that polymorphism of the apoA-I gene is inherited as a trait linked to premature atherosclerosis in one affected family. Ordovas et al. have also shown that the apolipoprotein A-I gene polymorphism was associated with CAD in a study of 88 patients, and was also found in 8 out of 12 kindreds with familial hypoalphalipoproteinemia. Finally, the possible association between NIDDM and arteriosclerosis is further suggested by a recent report of an association between a apoA-I gene polymorphism and susceptibility to NIDDM.

Because of the distinct possibility that the next several years will lead to greatly increased availability of genetic markers and likely specific gene loci with documented association with CVD, it is of interest to study these in the Indian groups to be examined in the current survey. The present study will undoubtedly include many related people and gives the opportunity to identify families for linkage studies. For this reason, it is proposed in the present protocol to isolate and store DNA from lymphocytes of blood sample. This can be easily accomplished in an efficient and economical way and would, therefore, serve as a store for future genetic studies.

1.6 PROCEDURE FOR GLUCOSE TOLERANCE TEST (GTT)

For all subjects, a fasting glucose value will first be obtained by using One-Touch (see Volume III Laboratory Procedure for details). Query subjects as to whether they are a known diabetic. If they are, ask if they take insulin or oral agents.

Note that all diabetic participants taking insulin will be exempted from the glucose tolerance test (GTT). Those diabetics who take oral agents and who have two random glucose values ≥ 250 mg/dl. or any participant with a fasting glucose ≥ 225 mg/dl. by One-Touch will also be EXEMPTED from the GTT. For individuals on renal dialysis or who have had a kidney transplant, blood will be drawn at the time of the examination, if possible.

1. Have the bottle of glucose (Glutol 75g.) and blood drawing equipment ready. Although the Glutol has proved to be very dependable and consistent when its concentration per ml has been measured in numerous samples, the volume supplied per bottle is not consistent. Thus it is necessary to measure both the Glutol and the water into which it will be diluted for each patient. The easiest way to accomplish this is to have a plastic graduated container such as that used for urine collections. The person administering the glucose tolerance test can thus pour 135 ml of Glutol into the measuring container, pour that into the cup supplied to the patient and then measure out 135 ml of water using the same measuring container. The cup containing the diluted Glutol is then ready for the patient. This measuring container can be used for all patients visiting on that day, but it should be discarded at the end of the day and a fresh measuring container used for the next clinic.
2. Ask subject if he/she has been fasting for 12 hours and whether he/she has refrained from smoking and beverages other than water, and record the response on the GTT check list given in Appendix C.

3. Draw fasting blood samples as described in Procedure for Blood Drawing. Record the time of blood collection.

4. Describe the purpose of the GTT to the subject.

5. Ask the subject to drink the glucose solution quickly, within 3 minutes - Record the time the process started on form.

6. Instruct the subject that he/she should not eat, drink or smoke anything until the second blood sample is obtained two hours later.

7. Instruct the subject to take the specimen container to the bathroom for the urine sample - Record the time of urine collection.

8. Place urine sample in the refrigerator.

9. Obtain second blood sample at exactly 2 hours post load - Effort should be made so that the second blood sample is obtained at exactly 2 hrs ± 3 min. Record the time of collection.

1.7 PHYSICAL EXAMINATION

During the examination, participants wear a gown, or loose fitting clothes that do not impair accurate body measurements and the examination. It is helpful to have them wear large scrub pants to enable the pant legs to be rolled up for the ECG examinations. Shoes and socks are removed for the supine examination and weight and height measurements. The form to be used is given in Appendix C.

1.7.1 Anthropometry

Anthropometry is performed before the clinic snack with the participant's bladder empty. The subject may wear a scrub suit or clothing into the station. Measurements may be taken over the scrub suit or light clothing only. Make sure that the pockets are empty and the belt is removed. Height and weight measurements are not to be taken with the participant wearing shoes.

Measurements, if possible, are taken by a team of two persons (one acting as observer, the other as recorder). If two are available, the first observer takes the measurements, calling out the value of the measurement.

The first observer keeps the measuring instrument in place until the recorder repeats the number. The recorder also checks the examinee's position during the procedure. If a single observer performs the
measurements, each should be recorded immediately after they are taken. Values taken are rounded to the nearest unit indicated for each measure. Fractions less than 0.5 will be omitted and fractions greater than or equal to 0.5 will be rounded up to the next higher unit.

1. Height and Weight

a) Standing Body Height

The participant stands erect on the floor or the horizontal platform with his/her back against the vertical mounted ruler, heels together and against the vertical ruler, looking straight ahead with his/her head in the Frankfort horizontal plane (the horizontal plane which includes the lower margin of the bony orbit and the bony socket containing the eye the most forward point in the supratragal notch just above the anterior cartilaginous projections of the external ear) (Figure 1). The right angle is brought down snugly but not tightly on the top of the head. A foot stool is used if the examiner is shorter than the participant so that the examiner's view is level with the point of measurement on the head of the participant. The participant's height is recorded to the nearest centimeter using the rounding method described above. The participant is instructed to stand as straight as possible but with feet flat on the floor. (A check is made to be sure the floor is level, the wall is at a 90 degree angle to the floor, the wall is straight and the metal ruler is mounted perpendicular to the floor). A chart converting centimeters to inches is on the wall or available for use in informing the participant of his/her height in inches.

b) Body Weight

Before a participant is weighed, the scale is balanced so that the indicator is at zero when no weight is on the scale. The scale must be level and on a firm surface (not a carpet). The participant is instructed to stand in the middle of the platform of the balance scale (Detecto, model 683-p) with head erect and eyes looking straight ahead. Record the results to the nearest kilogram using the rounding method described above. To maintain accuracy, the scale is zeroed daily and must be calibrated with a known weight (50 lbs.) every month or whenever the scale is moved. To calibrate the scale, check that the 50 lb. weight weighs 50 lbs. after zeroing the scale. Furthermore, the operator should make sure that an adult must weigh 50 lbs. more when standing on the scale holding the weight.
Figure 1. Frankfort Plane for Measuring Body Height

Figure 1 (a). General Description: The scapulae, or shoulder blades, are large, triangular, flat bones situated in the dorsal part of the thorax between the levels of the second and seventh ribs. A sharp ridge, the spine, runs diagonally across the posterior surface of the flattened, triangular body. The end of the spine projects as a flattened, expanded process called the acromion. This process articulates with the clavicle.

Figure 1 (b). the Frankfort Plane: The horizontal plane which includes the lower margin of the bony orbit, the bony socket containing the eye and the most forward point in the supratragal notch, the notch just above the small prominence of skin covered cartilage projecting over the meatus of the external ear.
2. Supine Waist (Abdominal) Girth

An anthropometric tape is applied at the level of the umbilicus (navel) with the patient supine (Figure 2) and the participant is instructed to "breathe quietly". The measurement is made and recorded to the nearest centimeter using the rounding method described above.

3. Erect Hip Girth

Instruct the participant to stand erect yet relaxed with weight distributed equally over both feet. The hip girth is measured at the level of maximal protrusion of the gluteal muscles (hips) (Figure 3). Keep the anthropometric tape horizontal at this level and record the measurement to the nearest centimeter using the above rounding method. Only one measurement is made. The greatest source of error for this measurement is due to not having the tape horizontal. Technician(s) should check the position of the tape to assure its correct position from both the front and back.

4. Upper Arm Circumference

The participant sits on a table or stool so that the right arm hangs freely with the right hand resting on the right knee. The observer applies the tape measure horizontally at the midpoint between the acromion and olecranon (Figure 3). Record the measurement to the nearest centimeter using the rounding method described above. This measurement is used to select the proper size blood pressure cuff.

A Novel Products tension tape is used to measure both abdominal and hip girth and the upper arm circumference.

1.7.2 Training and Certification for Anthropometry

Each technician must undergo training and certification by an experienced anthropometrist. The training program for taking body size measurements consists of the following components.

1. Training is conducted centrally by an expert in anthropology.

2. Each field center trains one or two individuals before the baseline examination. One individual from each center is designated the center's anthropometry supervisor.

3. If additional personnel are needed by a center to perform anthropometry, training is provided by the center's anthropometry supervisor.

4. Training includes:

   a. Introduction - rationale for body size measurements, overview of technique, expected limits of reproducibility, and pitfalls related to anthropology.
b. Demonstration of technique - an expert demonstrates the proper technique of each measurement on a volunteer subject. This includes a description of proper and improper techniques, as well as recording of data.

c. Practice - technicians divide into groups of three, and two techs perform measurements on the third in a round-robin fashion. This is done under the observation of a trained anthropometrist. Differences in technique and clarification of problem areas are discussed.

d. Testing - several subjects are assessed independently and blindly by each technician. Each technician's measurements are compared with the expert's measurements and the results discussed in class. The four subjects examined have four distinctly different body types: lean, obese, athletic, and aged.

e. Certification - technicians must measure one or more test subjects and be within certain standards of error:
1) The arm, waist and hip measurements must agree within ± 1 cm on each subject.
2) Weight must agree within ± 1 kg. Height within ± 1 cm.

If these are met, the subject receives certification for field work. Trainees who have problems are identified, and they are allowed to practice and try again to be certified.

1.7.3 Sitting Blood Pressure

1. Introduction

In the Strong Heart Study, sitting blood pressure is measured in a resting state, using 3 measurements with a Baum mercury sphygmomanometer. Within any one individual, variation in blood pressure is substantial, even within a few minutes and particularly under conditions perceived as stressful. Use of three replicate readings tends to reduce this short-term variation.

2. Standardized Clinic Procedure

Correct measurement of blood pressure is of the utmost importance to the success of this study. It is essential that the procedure described below for measuring blood pressure be followed exactly. Precision is essential for valid comparisons of blood pressure between groups of people and in individuals on different occasions.
Figure 2. Location of Waist Girth Measurement

Supine waist girth at level of umbilicus
Figure 3. Location of Upper Arm, Hip, and Calf Circumference

Upper Arm Circumference

Hip Girth (at maximum protrusion of gluteal muscles)
3. Description of the Equipment

a) Stethoscope

A standard stethoscope with a bell is used. Korotkoff sounds are best heard with the bell because of their low pitch. Stethoscope tubing should be about 10-12 inches from the bell piece to "Y" branching. This length provides optimal acoustical properties and allows the observer to read the sphygmomanometer at eye level and in a comfortable position. Earpieces should fit comfortably and snugly in the ears. Four points should be observed in using the stethoscope.

i) The ear piece should be directed downwards and forwards into the external ear canal.

ii) The ear pieces should be tight enough to exclude outside sound but not so tight that they cause discomfort.

iii) The valve between the bell and the diaphragm should be turned in the correct direction.

iv) The bell of the stethoscope should be placed lightly on the skin overlying the brachial artery - immediately below the cuff and medial to the cubital fossa above the medial epicondyle of the radius and posterior to the biceps muscle. Light pressure accentuates the low-pitched sound and avoids compression murmurs. When pressing too heavily with the bell on the artery a murmur can be heard which may prolong the apparent duration of phase 4 and give inaccurate readings.

b) Sphygmomanometers

Standardized Baum mercury instruments are used for all clinic visits. The mercury manometer consists of a screw cap, a face with numbers, a lined glass column, a reservoir containing mercury, rubber tubing, and a metal case. The rubber tubing from the mercury manometer connects to the rubber tubing from the inflatable rubber bladder of the cuff. As the inflatable rubber bladder is filled with air, the air pressure in the bladder travels through the connecting rubber tubing. The pressure pushes the mercury out of the reservoir and into the lined glass column. The number for each line is read when the rounded top of the mercury, the meniscus, is level with it. If the meniscus is exactly between the lines, the reading is made from the line immediately above, i.e., rounded up to the nearest even number.

c) Cuffs and Bulbs

Proper size of the cuff is essential for accurate blood pressure measurement. Study Centers have three standardized Baum cuffs available - adult, large adult, and thigh cuff.
The range markings on commercial cuffs overlap from size to size and do not offer a precise guideline. In the Strong Heart Study arm size is measured and the cuff size is selected as follow:

<table>
<thead>
<tr>
<th>Cuff Size</th>
<th>Arm Circumference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult</td>
<td>24 to 32 cm</td>
</tr>
<tr>
<td>Large Adult</td>
<td>33 to 41 cm</td>
</tr>
<tr>
<td>Thigh</td>
<td>&gt;41 cm</td>
</tr>
</tbody>
</table>

4. Blood Pressure Measurement Instructions

Some of the many extraneous factors influencing blood pressure are controlled by standardizing the measurement technique and the environment in which the measurement is made. Uncontrolled factors, such as time of day, arm circumference, recent use of caffeine, and identity of the observer are recorded, so that they can be taken into account during analysis.

The Strong Heart Study participants are asked to avoid caffeine (tea, coffee, chocolate, and soft drinks), eating, heavy physical activity, smoking and alcohol intake for twelve hours and to refrain from smoking for at least one-half hour prior to the clinic visit. Current drug intake, including medications affecting blood pressure, and non-prescription drugs is recorded on the day of the examination. A detailed history of alcohol intake and recent physical activity at work and leisure are also recorded.

5. Staff Preparation for Participant Visit

In relating to the Strong Heart participants, remember that participation in the study is voluntary. Participants are given full explanation and instructions about the preparation for the blood pressure examination and an opportunity for questions. The setting in which blood pressure measurements are made is standardized.

6. Measurement Procedures

The sitting arm blood pressure is measured three times at each clinic visit. It takes approximately 10 minutes to make three blood pressure measurements including the initial five minute rest. The blood pressure measurements are made early in the clinic visit sequence immediately following the reception and informed consent, and more than 15 minutes after phlebotomy.
Once the participant is given instructions and explanations, and the equipment has been checked, blood pressure measurement begins. The following steps must be followed precisely.

a) If the participant indicates that there is a medical or postsurgical reason for not having the blood pressure measured on the right arm (or if the right arm is missing), reverse chairs and proceed with the left arm. Indicate on the data collection form that the left arm is used. If in doubt, or if the participant prefers not to have a blood pressure taken on either arm, consult with the supervisor.

b) Seat the participant with the right arm on table. The bend at the elbow (ante-cubital fossa) should be at heart level. Legs should be uncrossed and head support comfortable. The participant should be able to relax the neck and shoulder muscles as much as possible.

c) Record the time. Allow a five minute wait before taking the blood pressure. Conversation should be limited. However, a brief explanation of the procedure can be repeated at this time if necessary.

d) Connect the cuff to a standard manometer and establish the pulse obliteration pressure by slowly inflating while palpating the radial artery until pulse is no longer felt. Deflate and record the pulse obliteration pressure. Raise the arm for 5 seconds and wait at least 25 seconds before auscultating the blood pressure.

e) Palpate the brachial artery (just medial to and above the ante-cubital fossa), and mark this location for stethoscope placement. Choose the correct cuff size and wrap the cuff on the arm with the center of the bladder over the artery.

f) Measurement 1: Connect the cuff to the manometer. Inflate rapidly to the pulse obliteration level + 30 mm. Holding the pressure constant with the bulb, wait 5 seconds. Place the bell of the stethoscope on the brachial artery and slowly deflate the cuff (2 mm per second) while listening. Record the 1st and 5th phases, reading the pressure in mmHg to the nearest even number. The first sound heard in a series of at least two sounds is recorded for systolic blood pressure (phase 1). The first silence in a series of at least two silences is recorded for diastolic blood pressure (phase 5), not the last sound heard. If the sounds do not cease completely, the fourth Korotkoff sound will be used. If the mercury column falls in between two scale marks at the time the first or fifth Korotkoff sound is heard, the higher number should be used.

g) Measurements 2 and 3: Have the participant raise measurement arm for five seconds. After waiting another 25 seconds with the participant’s arm on the table, repeat the measurement in step f above and disconnect cuff.
Average blood pressure readings are calculated for the second and third readings. Because of the importance of the blood pressure averages, to inform the participant and for the purposes of referral, all arithmetic is done with a calculator.

If for any reason the observer is unable to complete, or has forgotten to complete any portion of the examination (and the participant is gone), draw two horizontal lines through the space(s) on the form. This is the correct way to indicate missed information. If an entire reading is missed and the participant is still sitting at the blood pressure work station, completely deflate the cuff and start over with a replacement reading.

7. Reporting the Blood Pressure Results to the Participant

Using a calculator, average the second and third readings and mention the results to the participant. State clearly the systolic and diastolic pressure.

8. Procedure for changing the peak inflation level

Occasionally the Korotkoff sounds may be heard as soon as one places the stethoscope over the brachial pulse. If this happens, the peak inflation level used was too low. The observer immediately deflates the cuff by releasing the thumbscrew and disconnecting the cuff tube. Then have the participant hold the cuff-wrapped arm vertically for five seconds. Proceed with blood pressure measurement, starting at a new peak inflation level, 10 mmHg above the previous level.

9. Sitting Blood Pressure Training and Certification

At each field center a minimum of two clinic staff persons are trained for measuring sitting blood pressure. They need not be health professionals, but they must be trained and certified in the blood pressure measurement technique. Observers should also have experience in relating to people.

The first training session begins with a description and demonstration of the correct blood pressure measurement procedure. Trainees watch the American Heart Association blood pressure instruction video tape. Checklist is used for certifying all persons taking BPs (Appendix A3). Simultaneous BPs will be recorded using a Y stethoscope as described in Appendix A4.

It is the responsibility of each field center to conduct these procedures and report to the Coordinating Center when the procedures are completed.

Y Tube stethoscope observations are made in conjunction with the blood pressure training video during initial training and for quarterly quality control. The trainer has the observer-trainee go through the entire blood pressure measurement procedure using a quality control checklist. The observer and trainer listen with the Y Tube and record the values on separate sheets. Two measurements on one subject are obtained. Measurements by the trainer and the trainee should agree within 4 mmHg on any one reading (systolic or diastolic) and averages should agree within 3 mmHg.
10. Quality Control

To ensure the accuracy of the blood pressure measurements throughout the study, quality control measures are developed centrally and applied at all field centers. These measures include:

a) recruitment of the most qualified personnel
b) standardized training and certification
c) retraining as necessary
d) observation of data collection by supervisors, using the checklist given in Appendix A4. One checklist is used for each technician and mailed to the Coordinating Center each month
e) frequent staff meetings to provide feedback
f) editing of data, both manual and by computer
g) a quality assurance program administered by the Coordinating Center
h) simultaneous Y Tube observation of each technician by the blood pressure supervisor
i) equipment and maintenance program

11. Technician Training and Quality Control

Blood pressure technicians are trained centrally prior to participant recruitment. New technicians hired after the start of the study are trained locally by the Study Coordinator or a designated "Blood Pressure Supervisor".

The Coordinating Center directs a blood pressure quality assurance program to review six-monthly data. This includes quality analysis and review of blood pressure data every 3 months, comparing means for each technician with the values for all technicians, by center. These statistics are adjusted for weight, age and sex of the participants by the use of Z-scores. Arbitrary levels of Z-scores, (which can be modified according to performance) are used to detect possible systemic deviations in blood pressure measurement by individual technicians. Digit preference is also monitored for each technician. The Form for Recording Simultaneous Blood Pressure Observations in Appendix A4 will be used.

12. Equipment Maintenance

Each study center is responsible for the proper operation and maintenance of its equipment. Maintenance responsibility is assumed by the nurse clinician, and all staff are instructed to report any real or suspected equipment problems to that person promptly.

All checks, inspections, cleanings and problems indicated are documented and recorded by date in a permanent log. Problems and solutions are also recorded. The local nurse clinician sends a copy of this log monthly to the Coordinating Center. A copy of this log is given in Appendix A5.
The standard sphygmomanometer is inspected once a month. These inspections include a check of:

i) the zero level
ii) mercury leakage
iii) manometer column for dirt or mercury oxide deposit
iv) condition of all tubing and fittings

The equipment is cleaned if inspection indicates it is needed, or at least once a year. Specific maintenance instructions for the standard sphygmomanometer are provided in Appendix A6.

1.7.4 Ankle Systolic Blood Pressure

1. Move the Participant to the Supine Position

Assist the participant in moving to the supine position on the examination table.

2. Applying the Blood Pressure Cuff

The appropriate ankle blood pressure cuff is applied on the right calf. The same size cuff should be used on the ankle as the one used on the arm. In special instances, different cuff size may be used.

At this point, a blood pressure cuff is applied above the ankle of the right leg, as shown in Figure 4. Place the cuff flat on the table (the surface marked "side to the patient" face up) with the appropriate ankle centered on the cuff. At this time disregard the "over the artery" marker. The lower edge of the cuff (from which the hoses extend) should be approximately 2 to 2 1/2 inches above the medial malleolus. Following the contour of the lower leg, wrap the end of the cuff with the velcro "fabric" over the ankle, as shown in Figure 5. Note that depending on the degree of tapering in this area, the cuff corner will be offset from parallel toward the knee. Holding the cuff from sliding, wrap the other end over the ankle (step III in Figure 5), again following the contour of the ankle, and secure the velcro. Check to be sure that the corners of the cuff extending above the upper edge of the cuff are about equal: if one end extends more than the other, loosen the velcro and adjust the wrap. Next, locate the "over the artery" marker of the cuff, and rotate the cuff so that this line is directly over the posterior tibial artery. The cuff may be rotated more easily by sliding it toward the malleolus, and after alignment, the cuff can be made snug by pulling it up toward the calf. The cuff should conform closely to the shape of the ankle, with the lower edge 2 to 2 1/2 inches above the malleolus.

The posterior tibial artery is usually palpated as it courses posteriorly to the medial malleolus. Even if the posterior tibial pulse is not palpable, the posterior tibial artery is used as the location for the marker line on the cuff for the "over the artery position". Any kinks in the tubing are removed, and any "tugging" of the tubing on the participant's leg is relieved.

3. Procedure for Measuring Ankle Blood Pressure

a) Palpate posterior tibial pulse and mark these locations. Apply ultrasound gel to the posterior tibial area over the pulse or in the area shown on Figure 4.
b) Listen for the pulse using the Imex Mascot Doppler. If no pulse is audible or palpable, then try to use the dorsalis pedal pulse for the determination of blood pressure. If no pulse is audible, record zero for ankle blood pressure after the absence of pulse is verified by a second observer.

c) Inflate cuff to a pressure reading 20 mm higher than the "Peak Pressure" used for the sitting arm pressure (i.e., obliteration plus 50 mmHg) and utilize identical deflation techniques while listening with the Doppler.

d) Take a second blood pressure, and record both blood pressures in the Physical Examination Form. This procedure also applies to the doppler arm blood pressure.

e) Record the first sound as described above.

The blood pressure cuff is applied over the brachial artery according to the instructions found in the Sitting Blood Pressure section of this manual. By consulting the participant's Data Form, the observer verifies that the same arm and the same cuff size are used as for the sitting blood pressure readings.

If the participant had his/her sitting blood pressure taken on the right arm earlier in the clinic examination, the cuff is applied on the right arm at this time. The observer then uses the Doppler to record the brachial pressure. The pressure recorded in the right arm is used to calculate the brachial/ankle systolic pressure ratio for both lower extremities.

If it is impossible to obliterate the sounds after increasing the pressure to above 250 mmHg, no systolic measurement should be made in that ankle.

f) Repeat the procedure for the left leg and record the pressure as soon as the cuff is in the proper position.

The observer now removes all conduction jelly. Socks and a robe or other garments are now replaced and the participant is escorted to the next work station.

1.7.5 Electrocardiogram

1. Basic description

a) A Marquette Mac-PC (or Mac-12) based system will be used.

b) All ECGs will be transmitted centrally to the New York Hospital - Cornell Medical Center in New York electronically by modem.
c) All ECGs will be read in a standard manner at the ECG Reading Center by Board Certified or Board Eligible Staff Cardiologists and transmitted or mailed back to the site of origin for clinical correlation or other action, if required. In any case, all ECGs will be over-read and promptly returned.

d) All ECGs will be Minnesota coded at Cornell.

e) The Strong Heart Study will itself maintain a permanent copy of all cardiograms in its possession to assure "perpetual" availability of the study data for study members.

f) A standard level of competence must be demanded of our personnel performing ECGs at each site. A "competency exam" would be conducted of all persons recording ECGs at individual sites by a physician (or other designated person) who would judge the ability of the person being examined to adhere to standard protocol.

2. Minimal Equipment Requirements

a) A new Mac-PC with modem will be used at each clinic. Mac-12 machines may be used if they are available.

b) New York Hospital - Cornell Medical Center will provide free use of their mainframe MUSE (Marquette Universal System for Electrocardiology) system (except for study hook-up costs and paper costs) for the duration of the study. This system can be accessed 24hrs/day by modem and stores all study cardiograms together or by center. Also, floppy disc downloading can be accomplished to a Mac-12 compatible format.

Transmission instructions on Mac-PC and Standardized ECGare given in Volume IV of the manual.

Procedures will differ at each center concerning how ECG readings are supplied to local physicians and IHS health records. A copy of the ECG obtained at the time of performance, if marked "unconfirmed" can be included in the patients chart that day. A clinical reading will be performed at Cornell and returned by reverse transmission procedure WITHIN one week. A hard copy of this clinical reading will also be sent to the Coordinating Center for storage.

All ECGs will be Minnesota coded at Cornell. The Minnesota codes will then be added to the ECG data set by the Coordinating Center for data analyses.
Figure 4. Placement of the Blood Pressure Cuff on the Ankle
Step I. Positioning the Lower Leg on the Cuff
Step 2. Wrap fabric end of the cuff following contour of ankle

Step 3. Wrap and secure cuff

"ears" about equal
1.7.6 Impedance Measure

The measurement of body fat is accomplished using the Impedance Meter, Model # B1A101, made by RJL Equipment Company. This involves a small low frequency current which travels across the body through the extracellular fluids. The measurement of bioelectrical impedance is related to the volume of the conductor and when expressed as impedance or conductance, it is proportional to fat free mass.

1. Procedure

a) Before beginning, explain why you are making the measurement to the subject and check to see that the subject has not exercised vigorously for the past 12-hours and has not consumed alcohol in the past 24-hours. Make sure that the subject is not dehydrated. Record past vigorous exercise or alcohol consumption on the data form.

b) Before beginning the test, be sure that the subject cable is securely attached to the RJL spectrum, have the subject remove the right shoe and sock and lie down with the right side nearest to the analyzer;

c) If the examination table is metallic, it must have a foam pad - all of the body must be on the pad.

d) For best results:

i) Use electrodes only once.

ii) Legs should be far enough apart so that thighs do not touch each other. A towel may be used to prevent the legs and thighs from touching.

iii) Hands and arms should be far enough apart so that the arms and hands do not touch the torso. A towel can be used to prevent the arms from touching the body.

iv) No body parts should be in contact with any external metal (jewelry and pins in bones will not effect the results).

v) Subject's skin should be clean, dry and warm to the touch. If the skin is oily, clean it with an alcohol swab before attaching the electrodes.

Prior to the attachment, cut the electrodes in half bisecting the foil tab. The cut edge of the electrode placed on the ankle and wrist should face toward the shoulder and thigh respectively. The cut edge of the other two may face in either direction.
e) Electrode Placement:

i) Attach the black wires to the foot with the red clip connected to electrode at ankle (F1). Attach the red wires to the hand with the red clip connected to electrode at the wrist (H1).

ii) Put H1 on an imaginary line from the protruding bone of the wrist to bisect the ulnar head; make sure that the cut edge of the electrode is toward the shoulder.

iii) Put H2 just above the knuckles of the right hand or on any finger; there should be at least 5 cm difference between H1 and H2.

iv) Put F1 on an imaginary line between the protruding ankle bones to bisect the medial malleolus; make sure that the cut edge of the electrode is toward the thigh.

v) Put F2 just above the toes of the right foot or on the great toe (there should be 5 cm difference between F1 and F2)

Once the electrodes have been properly attached to the subject, the values for resistance and reactance will appear on the screen. Record these on the results sheet. Make sure that the toggle switch is set on x1.

2. Instructions for Impedance Meter

Battery Charging

Unit has rechargeable batteries that must be charged before use. They are charged by plugging instrument in with power switch in off position. Manufacturer suggests charging for 8 hours prior to use. Instrument should not be plugged in longer than 8 hours; damage to batteries may occur.

For our use they suggest the following: Plug unit in first thing in the morning before clinic and at least 15 minutes before the first test. Leave unit plugged in for the duration of each clinic, but have the power on only when testing a patient. At the end of clinic, the meter should indicate high charge (green area).

Checking Instrument

Before testing the first patient, be sure that the cables are not crimped or damaged. Check battery charge using the following procedure. Disconnect power cord. Place the Resistance/Reactance switch in the resistance position. Place the switch labeled x1/x10 in the x1 position. Attach the 2 clips from one patient cable to one side of 500 ohm resistor provided.
Attach the two clips from the other cable to the other side of the resistor. Turn power on. Resistance displayed should be between 490 and 510 ohms. If resistance is in this range, proceed with patient testing.

If resistance is not within this range, the batteries may not be fully charged, or another problem may be present. If charge appears to be low, charge batteries for 8 hours, then retest. If unit is fully charged and resistance is still not acceptable, see Impedance Tech Manual, page 9, for trouble shooting.

Note: Patient cables are made of silver. Take care not to bend or abuse cables. They should be left plugged into instrument to minimize handling, except when relocating instrument.

3. Quality Control for Impedance Measure

Training for the measurement of body fat using the bioelectric impedance meter was accomplished by an experienced nurse to demonstrate the following steps:

a. Instructions concerning the use and verification of the machine.

b. Demonstration by instructor of the procedure.

c. Practice by the individual operators.

d. Certification of operators if instructor and operator achieve an impedance measure where resistance and reactance were each within 3%.

For ongoing quality control in each center, one individual will be designated as supervisor of the impedance measures. This individual will assure that each of the other operators of the instruments is re-certified quarterly by having him/her perform an impedance measure on the same individual as the instructor. These should agree within 3%.

In addition, the instructor is responsible for the monitoring of the impedance meter. This includes checking the battery charge daily before the instrument is used, following the instructions in the manual. Further, the instructor should observe individual operators performing impedance measures at least quarterly to verify consistent and proper technique.

1.7.7 Examination of the Pulse

a) Ankle Edema

The socks or other foot covering are removed. The participant is examined in the supine position. Gentle but firm pressure is applied along the mid-tibia, anteriorly down to the ankle in each leg. Pitting or indentation remaining after pressure is removed constitutes definite edema. The examiner identifies the mid-point between the
prominence of the medial malleolus and the inferior border of the patella. Pitting at or above that mid-point is recorded as "marked" edema. Pitting only below that point is recorded as "mild" edema. The degree of edema is based on the extent.

b) Posterior Tibial Pulse

The examiner palpates inferior to the medial malleolus of each foot. The presence or absence of arterial pulsation is recorded. If in doubt, the examiner compares with the radial pulsation.

c) Dorsalis Pedis Pulse

The superior aspect of each foot is palpated for the presence or absence of this pulse.

d) Peripheral neuropathy using mono-filaments.

1.7.8 Physical Findings to be Confirmed by a Physician to Assure Presence of CHF

The participants should be referred for evaluation by a physician if these findings were noted so they can be confirmed and evaluated for the presence of congestive heart failure.

Bilateral ankle edema, orthopnea or paroxysmal nocturnal dyspnea.

The standard IHS referral form should be used to refer patients with newly observed physical findings described above to an internist or cardiologist so that the diagnosis can be confirmed and the prevalence of congestive heart failure can be determined. In such cases, use the Physician Referral Form for Diagnosis of CHF in Appendix A10.

1.8 Referral Guidelines

It is the intention of the Strong Heart Study that individuals who participate in the physical examination will be provided both with education and encouragement concerning a healthy life style aimed at preventing cardiovascular disease and, also that the participants receive assistance in securing medical care for any significant medical conditions uncovered during the course of the study exam.

1. Referral procedure:

a) All participants reporting for the medical exam will receive appropriate educational materials concerning a heart healthy lifestyle. In addition, the examining personnel, when possible, will endeavor to educate the participants during the exam concerning the importance of risk factor reduction and modifications that the individual might make to improve his/her risk for cardiovascular disease.
b) After all laboratory results are completed from the physical examination, a follow-up letter will be mailed to each participant thanking him or her for participation and supplying him/her with basic medical information obtained during the exam. (See example of letter and suggested interpretation in Appendix A7 and A8).

c) After all results from the medical examination are complete, a form will be generated by the Coordinating Center which will be available to the Indian Health Service for insertion into the patient's medical record. This will contain results of the electrocardiogram, carotid ultrasound measurements of body fat, glucose tolerance test, and blood measurements, which might be of benefit for their future medical care.

d) In order to insure that the patient receives appropriate referral and treatment for significant medical conditions uncovered during the course of the study, consistent referral levels have been established as described below which will be applied at each center.

2. Referral Levels and Medical Data Review

The Strong Heart Study refers participants using established guidelines for referral. Uniform criteria for referral of participants are implemented at all centers. Emergency, immediate, urgent, and routine referrals are made. Methods for referring participants who have no physician are established with the participant. All referrals are documented on a separate log and copies of the referrals are kept in the Strong Heart Study folders. The following are the levels of referral established for the Medical Data Review.

a) Emergency Referral: The patient is immediately escorted to a physician, an emergency squad or an ambulance is summoned. In such situations study personnel will provide emergency care to the best of their ability and training as appropriate to the emergencies that arise.

b) Immediate Referral: The participant is urged to see his/her physician within one day.

The SHS staff notifies the participant's physician or nearest IHS facility and makes appropriate arrangements for SHS participants to be seen that day. The participant is provided with an IHS referral form to take to his/her physician and transportation is provided or arranged if needed.

c) Urgent Referral: The participant is urged to see his/her physician within one week and SHS staff makes an appointment for needed follow-up whenever possible.

An IHS referral form is filled out and transportation is arranged if needed.

d) Routine Referral: The participant is asked to see his/her physician within one month, or at first convenient appointment and appointments for the patients are made by the CHRs
or clinic staff. An IHS referral form is filled out and transportation is arranged if needed.

e) No Referral: The study results are summarized for participant and the participants are advised that the summary of the final results will be mailed to them at a later date.

3. Referral and Review Guidelines for Independent Patient Follow-up

Guidelines for referral are provided in the table below. The SHS nursing determines the acuteness of the findings, as well as whether or not the condition is being followed by a physician.

If the participant is aware of and being followed medically for a condition, judgement is exercised about whether to refer. The standard IHS referral form is used to provide appropriate clinical information to the health care professional who will evaluate the patient. A copy of this referral will be retained with the research forms to document the referral that was made.

Referral at the time of examination

<table>
<thead>
<tr>
<th>Emergency Referral</th>
<th>Statement to Participant</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP ≥ 260 mmHg</td>
<td>Your BP is very high</td>
</tr>
<tr>
<td>DBP ≥ 130 mmHg</td>
<td>Your BP is very high</td>
</tr>
<tr>
<td>Any finding or symptom suggestive</td>
<td>Describe rationale for referral to participant</td>
</tr>
<tr>
<td>of a life-threatening illness, including evidence of acute MI, unstable angina, or pulmonary edema.</td>
<td>Use Local IHS Referral Form</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Immediate Referral</th>
<th>Statement to Participant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting One Touch glucose &gt; 400</td>
<td>Your blood sugar is very high</td>
</tr>
<tr>
<td>SBP 200-259 mmHg</td>
<td>Your BP is very high</td>
</tr>
<tr>
<td>DBP 105-129 mmHg</td>
<td>Your BP is very high</td>
</tr>
<tr>
<td>Diabetic foot ulcer</td>
<td>Your foot must be seen by a physician</td>
</tr>
<tr>
<td>Angina in last day</td>
<td>Your chest pains may be important</td>
</tr>
<tr>
<td>Neurologic symptoms in past week</td>
<td>Your symptoms may be important</td>
</tr>
<tr>
<td>Other severe symptoms or findings</td>
<td>Your symptoms may be important</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>-------------------------------</td>
</tr>
<tr>
<td>Untreated asthma or worsening asthma</td>
<td>You may have a serious problem in your lungs</td>
</tr>
<tr>
<td>Carbon monoxide reading &gt; 125</td>
<td>Your carbon monoxide level is very high (Also refer to IHS Environmental Health)</td>
</tr>
<tr>
<td><strong>Urgent Referral</strong></td>
<td><strong>Statement to Participant</strong> (&lt;i&gt;&quot;Consult M.D. within a week&quot;&lt;/i&gt;)</td>
</tr>
<tr>
<td>---------------------</td>
<td>-------------------------------------------------------------------</td>
</tr>
<tr>
<td>Angina over 24 hours ago</td>
<td>Your chest pains may be important</td>
</tr>
<tr>
<td>Neurologic symptoms, untreated, one week to six months ago</td>
<td>Your symptoms may be important</td>
</tr>
<tr>
<td>Suspected congestive heart failure (Use Local IHS Referral Form)</td>
<td>Your symptoms may be important</td>
</tr>
<tr>
<td>Other acute, but less severe symptoms</td>
<td>Your symptoms may be important</td>
</tr>
<tr>
<td>Inappropriate medication usage</td>
<td>Taking medication incorrectly may be dangerous</td>
</tr>
<tr>
<td>Non-diabetic with a fasting One Touch glucose of $\geq 200$</td>
<td>Your blood sugar is high</td>
</tr>
<tr>
<td>Chronic cough, fever, weight loss, and other symptoms suggestive of active TB or valley fever</td>
<td>You may have serious problem in your lungs</td>
</tr>
<tr>
<td>Carbon monoxide 20-124 for non-smokers 50-124 for smokers</td>
<td>Your carbon monoxide level is high (Also refer to IHS Environmental Health)</td>
</tr>
<tr>
<td>Carotid ultrasound findings indicate potential plaque/stenosis</td>
<td>You may have serious problem in your neck vessel(s)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Routine Referral</strong></th>
<th><strong>(&quot;Consult M.D. within one month or at first convenient appointment&quot;)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP 140-199 mmHg</td>
<td>Your BP is elevated into borderline range. Recommend that participant confirm blood pressure reading within 2 months</td>
</tr>
<tr>
<td>DBP 90-104 mmHg</td>
<td>Your BP is elevated into borderline range. Recommend that participant confirm blood pressure reading within 2 months</td>
</tr>
<tr>
<td>Old MI (Rose Questionnaire), previously unrecognized</td>
<td>Your chest pain may be important</td>
</tr>
</tbody>
</table>
Routine Referral
(Continued)
("Consult M.D. within one month or at first convenient appointment")

Neurologic problem (stroke, TIA findings) > 6 months ago, unrecognized

Your symptoms may be important

Claudication, previously unrecognized

Your leg pain may be important

Both pedal pulses are missing in one extremity and not previously referred or the ratio of doppler pressure of ankle/arm < 0.8

You may have a problem in your feet. You should check with your doctor

Undiagnosed peripheral neuropathy (Score 6 or less out of 10)

Your symptoms may be important

Referral after Results Are Available

1) Critical values: See next page for critical values of various laboratory results.

Laboratory will call field center. Field follow up is considered an urgent referral. SHS staff should notify participants by phone, home visit, or certified letter and should make an appointment for clinical follow-up within one week whenever possible. SHS staff should help arrange transportation if needed. An IHS referral form is filled out.

2) Routine report -- copies of routine results are sent to each participant with an interpretation of results. If the participants have new findings that they have not previously been advised of such as newly diagnosed diabetes, or cholesterol > 300, an IHS referral form should be filled out and SHS staff should assist participant in making an appointment and arranging transportation for follow-up (see letters and interpretation in Appendix A8).

3) Carotid Ultrasound -- the Cornell Reading Center will call the field center if > 50% obstruction is noted on the carotid artery. If the obstruction is ≥ 75%, the participant should be immediately referred for follow up. If the obstruction is between 50 and 74%, the participant should have a routine referral. If non-obstructive plaque (< 50%) is detected, the participant should be referred for risk factor assessment and counseling by his/her primary health care provider.
### Strong Heart Study Critical Values for Laboratory Results

<table>
<thead>
<tr>
<th>Test</th>
<th>Critical Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting Glucose</td>
<td>≤ 40  <strong>or</strong>  ≥ 400 mg/dl</td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>≥ 300 mg/dl</td>
</tr>
<tr>
<td>Total Triglyceride</td>
<td>≥ 1000 mg/dl</td>
</tr>
<tr>
<td>Plasma Creatinine</td>
<td>≥ 3.0 mg/dl</td>
</tr>
<tr>
<td>Na</td>
<td>≤ 125  <strong>or</strong>  ≥ 150 MEQ/dl</td>
</tr>
<tr>
<td>K</td>
<td>≤ 3.0  <strong>or</strong>  ≥ 6.5 MEQ/dl</td>
</tr>
<tr>
<td>Ca</td>
<td>≤ 8.0  <strong>or</strong>  ≥ 12.0 mg/dl</td>
</tr>
<tr>
<td>PO₄</td>
<td>≥ 6.0 mg/dl</td>
</tr>
<tr>
<td>Total Bilirubin</td>
<td>≥ 4.0 mg/dl</td>
</tr>
<tr>
<td>ALK</td>
<td>≥ 400 IU/L</td>
</tr>
<tr>
<td>BUN</td>
<td>None</td>
</tr>
<tr>
<td>Cl</td>
<td>None</td>
</tr>
<tr>
<td>CO₂</td>
<td>None</td>
</tr>
<tr>
<td>Uric Acid</td>
<td>None</td>
</tr>
<tr>
<td>Mg</td>
<td>None</td>
</tr>
<tr>
<td>AST</td>
<td>None</td>
</tr>
<tr>
<td>ALT</td>
<td>None</td>
</tr>
<tr>
<td>LDH</td>
<td>None</td>
</tr>
<tr>
<td>Total Protein</td>
<td>None</td>
</tr>
<tr>
<td>Albumin</td>
<td>None</td>
</tr>
<tr>
<td>CBC</td>
<td>Local IHS Laboratory critical values for CBC results will be followed</td>
</tr>
</tbody>
</table>
ECG REFERRAL: ECG Findings Requiring Review by M.D. before Participant leaves the clinic

Would like to review with M.D.,
Call should be made to Reading Center by field staff at (212) 746-4655

* Acute pattern abnormalities (MI, ischemia)

* Rhythm disturbances
  2nd or 3rd degree block, ventricular tachycardia,
  any type of ectopic beat > 6/minute, couplets bigeminy, R on T,
  multifocal premature ventricular contractions,
  atrial fib/flutter with ventricular rate < 60/min or > 110/min,
  sinus bradycardia < 40/min, sinus tachycardia > 110/min, PR interval ≥ 0.26 sec.

* Any other ECG findings, alone or in conjunction with symptoms, causing concern

Other ECG Findings to be reviewed the same day; if possible

QT Prolongation (confirm medications)

ECGs where Routine Referral is usually appropriate

  New left bundle branch block
  New right bundle branch block
  Wolff Parkinson White
  Left Ventricular Hypertrophy

Examples of Usually Benign ECGs (always obtain old comparison ECG when available)

  Left Axis Deviation/Left Anterior Hemi (Fascicular) Block
  Atrial Abnormalities, Intra-ventricular Conduction Delay
  Unusual P Wave Axis, Wandering Atrial Pacemaker
  S1, S2, S3 Pattern, Old Right Bundle Branch Block
  Incomplete Right Bundle Branch Block
  ST Elevation compared with Early Re-polarization
  First Degree AV Block

Copies of each ECG obtained as part of the Strong Heart Study will be forwarded to either the local clinical director or other identified local clinical personnel, if the participant consents to having results sent to the local IHS facility.
1.9 QUALITY CONTROL

1) Anthropometry and blood pressure

Duplicate measures of arm blood pressure (systolic and diastolic), ankle blood pressure, and anthropometry (height, weight, waist/hip ratio, and electrical impedance measurements) should be performed by a second observer on an approximate 5% randomly selected sample of participants. These data must be sent to the Coordinating Center for monthly analysis. Results of the analysis will be provided to the field centers and the Steering Committee on a monthly basis. Criteria for unacceptable differences are as follows:

1) Systolic Blood Pressure: 4 mmHg by Y-tube stethoscope
2) Diastolic Blood Pressure: 4 mmHg by Y-tube stethoscope
3) Height: 1 cm
4) Weight: 1.0 Kg
5) Waist circumference: 1 cm
6) Hip circumference: 2 cm
7) Resistance: 15 units

Duplicate data for blood pressure, height, and weight will be compiled by the Coordinating Center and reported to the clinics and Steering Committee quarterly; in addition, distributions of measurements and digit preference for each staff member will be compiled and repeated quarterly.

Anthropometric measurements and blood pressure by standard sphygmomanometer and by Doppler should be observed and evaluated quarterly by the clinic supervisor. This person will also assure that each of the other operators of the impedance meter is re-certified quarterly by having him/her perform an impedance measure on the same participant as the supervisor. In addition, a simultaneous Y-tube observation of each observer by the blood pressure supervisor should be made. All results will be analyzed by the Coordinating Center on a quarterly basis. Duplicate blood pressures taken by Doppler will be performed quarterly by the supervisor.

To maintain accuracy, the scale should be zeroed daily and should be calibrated with a known weight (50 lbs.) every month or whenever the scale is moved. The impedance meter should be calibrated daily, follow manufacturer's instructions. This includes checking the battery charge daily before the instrument is used. The standard sphygmomanometer should be inspected once a month. These inspections include a check of (i) the zero level, (ii) mercury leakage, (iii) manometer column for dirt or mercury oxide deposit, and (iv) condition of all tubing and fittings. Record equipment monitoring on a checklist. The Coordinating Center will compile the data and document staff performance.

2) Laboratory tests

Duplicate blood and urine specimens should be collected on approximately 5% of the participants and sent to the Core Laboratory in a blind fashion. Results obtained for each test will be
analyzed monthly by the Coordinating Center for accuracy and consistency. The percent of pairs with differences within 5%, 10%, and 20% will be computed. Correlation coefficients and coefficients of variation will be calculated and technical errors estimated. Poor correlation or unreasonably high technical error will be reported to the Laboratory and the Steering Committee.

3) Personal interview

   Personal interviews must be observed monthly by the study coordinator. Problems and errors should be identified using a checklist and corrected immediately.

4) Quality control for surveillance data

   See Volume I, Chapter 5, section 5.2 for details.

5) Quality control site visits

   Quality control site visits will be scheduled every six months. The site visit team which consists of the Program Manager from NHLBI and representatives from every center will visit each center, observe every component of the study, identify inconsistencies, discrepancies, and other problems, and provide advice for improvement.

6) Certification of technicians

   Each center will recruit the most qualified personnel. Clinical staff will be centrally trained and certified before the examination begins and newly hired personnel are trained at each clinic. Recertification occurs every six months to ensure accurate and consistent performance.

7) Confidentiality and safety of data

   All personnel with access to data collected for the study are required to sign a confidentiality pledge. Completed data forms are placed in locked file cabinets at every center and only authorized staff members have access to the data.