National Heart, Lung,
and Blood Institute

American Heart Association℠
Fighting Heart Disease and Stroke

Recommendations Regarding Public Screening for Measuring Blood Cholesterol

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Contents

SUMMARY/RECOMMENDATIONS

Since the initiation of the National Cholesterol Education Program (NCEP) and the development of simpler, more rapid laboratory measurements of cholesterol levels, screening for blood cholesterol levels has become widespread. Public screening has the possibility of detecting large numbers of individuals with high blood cholesterol levels in addition to those detected in the physician's office. However, if screening is to provide useful results, it must provide reliable measurement and ensure adequate education and followup.

Results of research on screening programs were presented at a National Heart, Lung, and Blood Institute (NHLBI) Workshop on Public Screening for High Blood Cholesterol in October 1988. The workshop participants suggested methods that could make public screening more effective in detecting high blood cholesterol in individuals who might otherwise not be identified in the health-care system and that could ensure followup of appropriate cases and public education about cholesterol. Recommendations for cholesterol screening programs were first issued by the National Heart, Lung, and Blood Institute and the American Heart Association in 1989. The present document is an update of these recommendations and contains information in new reports of the National Cholesterol Education Program, in particular, the second Adult Treatment Panel report (ATP II). One important recommendation is that measurement of high density lipoprotein (HDL)-cholesterol should be added to initial cholesterol testing. The current document updates previous screening guidelines by incorporating this new recommendation. But it also emphasizes that if HDL-cholesterol measurements are not available in the screening setting, measurement of total cholesterol levels still provides valuable information that can be utilized for cholesterol management.

The purpose of cholesterol screening is twofold: to augment the public health approach to cholesterol control and to support the clinical strategy. The first approach is designed to reduce the average blood cholesterol level in the general population, and this is accomplished by increasing public awareness of high blood cholesterol as a risk factor for coronary heart disease (CHD) as the initial step toward modification of life habits that lead to high cholesterol levels. Cholesterol screening is one important step toward increasing public awareness of high blood cholesterol. Cholesterol screening in young adults may be particularly valuable for making them aware of the need to modify life habits early in life to delay development of CHD for as long as possible in later life. The clinical approach aims to identify individuals who have elevated blood cholesterol or related disorders and who are candidates for cholesterol management in the clinical setting. If cholesterol abnormalities are detected in such individuals, they will appropriately be referred to their physicians for further evaluation.

RECOMMENDATIONS

Public screening must meet customary standards for recruitment of participants, reliable measurement of cholesterol level, the provision of appropriate information, staff training, and referral for further evaluation.

Public screening programs should:

- Use recruitment approaches that attract all adult segments of the community and develop special approaches to reach groups that would be underrepresented in usual detection programs. These include men, younger adults, low-income or low-education groups, and minorities.
- Adhere to all applicable requirements established under the Clinical Laboratory Improvement Amendments of 1988 (CLIA).
- Ensure precise and accurate cholesterol measurements. Public screening should meet the standards defined by the Laboratory Standardization Panel of the NCEP. Laboratory instruments to measure cholesterol should undergo prefield evaluation and should be subject to an ongoing system of quality control. As required by CLIA, a health professional must be available to fulfill the role of clinical consultant.
- Include education as part of screening by providing reliable verbal and printed information about cholesterol levels from knowledgeable staff. Simply telling a participant his or her cholesterol number is not sufficient in a screening program.
- Ensure that staff members have received training specific to their responsibilities, have access to consultation from appropriate health professionals, and have adequate supervision.
- Screening sites should be convenient, efficiently accommodate the numbers of screenees, be designed to ensure quality-control procedures, and ensure privacy.
- Provide cholesterol screening at a reasonable cost to the participant.
- Coordinate public screening with the local medical community by establishing liaisons with community health-care resources.
- Provide active referral and followup programs. The screening agency should be responsible for taking steps to increase the likelihood that referred screenees reach medical care. Followup methods such as letters or telephone calls are desirable.

Public screening programs should recommend referrals on the basis of the NCEP guidelines given below:

- Any person with a history of heart attack, chest pain indicative of angina pectoris, coronary bypass operation, coronary angioplasty, recurrent transient ischemic attacks (TIAs) or known blockage of a carotid artery, abdominal aortic aneurysm, or ischemic peripheral arterial disease should be referred to a physician for cholesterol evaluation, beginning with a complete lipoprotein profile (total, low density lipoprotein [LDL]-, and HDL-cholesterol, and triglycerides). Cholesterol screening in the public setting is not necessary or advisable.
- A total cholesterol (TC) of 200 mg/dL in an adult 20 years of age or older calls for referral to a physician for further cholesterol evaluation:
  - within 2 months if TC $\geq$240 mg/dL, or if TC is 200-239 mg/dL with two or more other CHD risk factors
  - within 1 year if TC is 200-239 mg/dL with fewer than two other CHD risk factors
- If an HDL-cholesterol measurement is available, a level below 35 mg/dL calls for referral to a physician for further testing. If an HDL test is not available, the individual should be reminded of the advisability of obtaining an HDL-cholesterol measurement. This test is especially needed if the person has other CHD risk factors (defined on page 14).
- If the HDL-cholesterol is 35 mg/dL or higher and total cholesterol is less than 200 mg/dL, cholesterol testing should be carried out again in 5 years.

INTRODUCTION/BACKGROUND

The congruence of many types of scientific evidence has led to general agreement in the medical community of the need to lower blood cholesterol to reduce the incidence of CHD. In 1985, the NCEP, a consortium of practitioners, public health professionals, voluntary health organizations, and government agencies, began a collaborative effort of professional and public education. In 1988, the Adult Treatment Panel of NCEP delineated guidelines for the detection, evaluation, and treatment of high blood cholesterol in adults. Treatment of individuals at risk cannot proceed, of course, until their cholesterol levels have been defined. Accordingly, NCEP advises adults: "Know your cholesterol number."

The second report of the Adult Treatment Panel II, released in 1993, updated recommendations for cholesterol management in adults. This report is similar to the first in outline, and it continues to identify LDL as the primary target of cholesterol-lowering therapy. However, the report contains three new features that distinguish it from the first. These include:

- Increased emphasis on CHD risk status as a guide to type and intensity of cholesterol-lowering therapy.
  - Identification of the patient with existing CHD or other atherosclerotic diseases as being at highest risk, and establishment of lower targets for LDL-cholesterol for these patients.
  - Addition of age to the list of major CHD risk factors, defined as $\geq$45 years in men and $\geq$55 years in women.
  - Recommendation of delaying the use of drug therapy in most young adult men (<35 years) and premenopausal women with LDL-cholesterol levels in the range of 160-220 mg/dL who are otherwise at low risk for CHD in the near future.
  - Enhanced recognition that high-risk post-menopausal women, and high-risk elderly patients who are otherwise in good health, are candidates for cholesterol-lowering therapy.
- More attention to HDL as a CHD risk factor.
  - Addition of HDL-cholesterol to initial cholesterol testing.
  - Designation of high HDL-cholesterol as a "negative" CHD risk factor.
  - Consideration of HDL-cholesterol levels in the choice of drug therapy
- Increased emphasis on weight loss and physical activity as components of the dietary therapy of high blood cholesterol.

The second new emphasis, more attention to HDL as a CHD risk factor, has important implications for cholesterol screening. Increasing scientific evidence indicates that a low HDL-cholesterol is a major risk factor for CHD. The purpose of HDL testing is to identify individuals who may have either a low or an elevated HDL-cholesterol, in order to improve initial CHD risk assessment and to guide later therapy. If the HDL test is available, it should be added to initial total cholesterol testing, providing that accuracy is assured. Although practical circumstances may dictate that cholesterol screening be carried out without the HDL-cholesterol

measurement, ATP II recommendations should be kept in mind, and screenees should be reminded of the importance of obtaining an HDL test in the future.

The NCEP advocates a dual strategy for lowering cholesterol levels in the general population. The first is the public health strategy, which encourages the general public to modify life habits with the aim of reducing CHD risk factors, including high blood cholesterol. This approach makes use of public education, governmental policy, and food industry actions to foster healthful changes in habits. The second approach is the clinical strategy, which attempts to identify high-risk individuals in the clinical setting. It is primarily a case-finding approach and is based on the premise that a large portion of the general population periodically passes through the clinical setting where the opportunity for appropriate cholesterol testing exists. Cholesterol screening outside the medical setting serves both the public health and clinical approaches. It assists in increasing the general public's awareness of the dangers of high blood cholesterol, while at the same time it facilitates the finding of new cases.

The NCEP guidelines, as well as the availability of portable chemistry analyzers that make cholesterol measurement rapid, affordable, relatively painless, and readily available, initially led to widespread screening outside the physician's office and enthusiastic public responses. Hospitals, nursing homes, health fairs, supermarkets, exercise clubs, and many nonmedical sites have provided screening for blood cholesterol. In addition, public screening has also become commercialized, with profit-oriented organizations selling these services. Recently, public screening activities appear to have declined, but there still exists a need to provide updated guidance on this subject.

In October 1988, the NHLBI sponsored a Workshop on Public Screening for High Blood Cholesterol to review and evaluate data from public cholesterol screenings and make recommendations for quality control, recruitment, referral, and education. Data were presented from NHLBI-supported community heart disease prevention demonstration projects, the Model Systems for Cholesterol Screening Program, and scientists working in the field. The workshop proposed objectives for public screening and made recommendations for achieving these objectives. This document updates the workshop guidelines in light of recent developments, including the recommendations of ATP II.

Objectives for Public Cholesterol Screening

- To detect individuals with high levels of blood cholesterol and make appropriate referrals to sources of medical care.
- To raise public consciousness and knowledge about the relation of blood cholesterol to CHD.
- To provide information about eating patterns and other approaches to achieve and maintain appropriate levels of blood cholesterol.
- To reach those who might not otherwise have their blood cholesterol measured as part of routine health care.

Research Findings and Recommendations

Recruitment of Screening Participants

An increased portion of the population know their blood cholesterol level and its relation to CHD risk. According to national surveys conducted in 1983, 1986, and 1990, the percentage of adults who reported ever having their cholesterol measured has increased from 35 to 65 percent, while the percentage who can report their own cholesterol number has increased from 3 to 37 percent. Nevertheless, the substantial proportion of people who do not yet know their cholesterol number necessitates continued detection and educational efforts.

Public screening can attract participants from all segments of the population. However, certain groups such as the elderly, women, white adults, those who are better educated or have higher incomes, and previously screened individuals are more likely to take advantage of screening opportunities. Conversely, men, younger and middle-aged adults, and those with low incomes or low levels of education may participate less frequently in public screenings. Minorities can be significantly underrepresented. The ability of public screenings to detect high-risk individuals in these underrepresented groups is currently limited without targeted efforts.

Targeted screenings at locations such as worksites and certain community locations can improve access for the groups mentioned above. Targeted screenings at multiple sites within a community can achieve a screening population representative of the whole, including high-risk groups.

As screening becomes more widely available, certain people will often return to repeat their blood cholesterol measurement. Between 25 and 40 percent of those attending a screening have had at least one previous assessment. This proportion will increase as more people are screened. Although rescreening for self-monitoring purposes may have some benefit, it can detract from work on undetected population groups and can promote reliance on screening as a surrogate for medical care.

Screening programs should utilize recruitment strategies that enhance participation by all population segments to ensure detection in those high-risk groups that are otherwise less likely to seek medical care.

Recruitment Strategies

Recruitment strategies should be constructed to take account of the following needs:

- Marketing approaches that emphasize participation of the entire adult population and that emphasize the underrepresented groups.
- Targeted screening at sites where underserved populations are found.
- Flexible hours at the screening site, including evenings and weekends, for maximum availability. Since testing for total cholesterol and HDL-cholesterol does not require fasting, flexibility in screening is further enhanced.
- Screening facilities that are accessible and affordable to all elements of the population.
- Recruitment of individuals unaware of their cholesterol level to enhance detection of new

high-risk cases and to discourage substitution of screening for medical care.

Analyzer Operation and Quality Control

Many desktop analyzers are available. Accuracy and precision of blood cholesterol measurements, which are critical for the classification and referral of screening participants, depend on appropriate quality control and staff training. However, even with these standards, it is inevitable that analytic and biologic variability will lead to some misclassification of individuals. Poor staff training and quality control could worsen the problem and lead to substantial misclassification. It should be stressed that a single elevated cholesterol measurement, even under rigorous quality control, does not establish the diagnosis of high blood cholesterol, for which two or more cholesterol measurements are needed. By the same token, a single low reading may fail to identify a person who is in need of professional cholesterol management. However, most screening participants will proceed to have a further cholesterol determination in a medical setting, and a major role of screening is to begin the process of determining the individual's cholesterol level. In any case, a repeat measurement within 5 years is recommended.

The premise that measurements meeting quality-control standards are possible in field settings is supported by a growing body of data. Reliable measurement is dependent on rigorous quality control and effective training of technical personnel. Internal quality-control procedures (regular analysis of known standards) and external quality-control procedures (comparative analysis of blinded samples with a reference lab) enable laboratory standards to be met. The cost of these quality-control procedures is estimated at 10 percent of analysis cost, which is modest compared with that engendered by excessive misclassification.

For HDL measurements, field experience with desktop analyzers is still limited, and a definitive statement about the reliability of fingerstick HDL determinations cannot currently be made.

Measurement Recommendations

Blood Sampling

- Either fingerstick or venipuncture samples can be used for total cholesterol. Good collection techniques should be observed.
- Blood obtained from either fasting or nonfasting individuals can be used for total cholesterol and HDL-cholesterol analysis.
- Differences in the measured concentrations of cholesterol in serum and plasma should be considered when reporting values. Referral should be based on levels adjusted to serum cutpoints as recommended by NCEP.
- The blood sampling procedures should be standardized to the sitting position if possible, preferably for at least 5 minutes, because postural changes can alter blood cholesterol concentrations.
- Cholesterol analysis should not be carried out in an individual with concomitant illness.

Analytic Devices and Laboratory Quality Control

- Desktop analyzers ideally should meet the performance standards of the NCEP Laboratory Standardization Panel, i.e., total error $\leq$8.9 percent. (One set of conditions that is consistent with this total error limit is:

  for accuracy - bias $\leq \pm$3 percent;

  for precision - coefficient of variation (CV) $\leq$3 percent.)*

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* Total error (TE) is calculated as follows:

TE = % bias + 1.96 (CV), or

TE = 3% + 1.96 (3%) = 8.9%

The expression {1.96 (CV)} represents the 95-percent confidence interval for the CV.

Accuracy is defined as proximity to the true value as determined by a reference method, and the coefficient of variation is an estimate of the reproducibility (or precision) of the measurement.

- Operators should be trained and able to demonstrate competence before screening (see page 9).
- Liaison with a certified clinical chemistry laboratory whose cholesterol analyses meet NCEP laboratory standards should be maintained for consultation and quality control.

Each analyzer should be evaluated and shown to demonstrate acceptable performance in the laboratory setting before field use. Individual instruments, even those from the same manufacturer, may differ in performance and calibration, and the quality of measurement for each machine should be established.

- This evaluation should include analysis of control samples that are traceable to the National Reference System for Cholesterol Measurements (NRSCM) established by the Centers for Disease Control and Prevention (CDC) and the National Bureau of Standards. Total cholesterol controls should have values that are near the decision levels of 200 mg/dL and 240 mg/dL.
- Multiple runs of these quality-control materials should be made in a laboratory during a 2-week period on 5 to 10 different days, and appropriate quality-control limits should be established for that instrument.
- Precision and accuracy should meet NCEP laboratory standards. *Analyzers not meeting these standards should not be used until appropriate corrective measures have been taken and documented.*

Field Quality Control (Internal Program)

- Screening programs should establish a continuous quality-control program that follows accepted laboratory principles and is adequate both to maintain and document performance. Control serum pools at two levels, near or bracketing the 200 and 240 mg/dL decision values, should be used. These are available from manufacturers or reference laboratories. They should be analyzed at the beginning of each screening day, after every 20 samples, and at the end of each day. If bias is outside the established control limits, the pool should be analyzed again, and if bias is still outside the established control limits, the instrument should be taken out of service until the problem has been corrected.
- Coefficient of variation and instrument bias should be calculated and logged weekly for each control pool. Instruments should receive appropriate corrective attention if these measures are outside NCEP guidelines.

Field Quality Control (External Program)

Screening centers may be either extensions of licensed clinical laboratories or independently licensed under CLIA.

- Screening centers that are extensions of licensed laboratories should make comparisons with the licensed laboratory on duplicate aliquots ("split" samples) drawn from a screenee or received as blinded samples sent from the licensed laboratory. One or two of these samples should be analyzed each day, and the values should be returned to the licensed laboratory. The accuracy of the licensed laboratory should be traceable to the NRSCM. This licensed laboratory must be part of a Health Care Financing Administration (HCFA)-approved proficiency testing program (e.g., College of American Pathologists proficiency surveys).
- Screening centers that are independently licensed under CLIA must participate in a HCFA-approved proficiency testing program (e.g., College of American Pathologists proficiency surveys). These screening centers are also encouraged to make comparisons with a licensed laboratory on duplicate aliquots ("split" samples) drawn from a screenee or received as blinded samples sent from the licensed laboratory. One or two of these samples should be analyzed each

day, and the values should be returned to the licensed laboratory. The accuracy of the licensed laboratory should be traceable to the NRSCM.

Remeasurement

- Screening values of total cholesterol above 300 mg/dL or below 100 mg/dL should be remeasured at the same sitting. The same is true for HDL-cholesterol values above 100 mg/dL or below 25 mg/dL.

Documentation

- Protocols documenting operating and trouble-shooting procedures should be kept with the instrument.
- An operations checklist should be provided and should be used by field personnel. A log should be maintained to document instrument problems and corrective action taken.
- Overall quality assurance of the testing process should be audited, and quality-control results should be logged and reviewed regularly by supervisory personnel.
- The screening team should maintain logs identifying all participants, their results, date of specimen collection, and any problems with specimens that may affect results. A copy of the test report must be maintained by the screening center for 2 years.
- Optimally, the instrument should provide hard copy readouts to minimize transcription errors and maximize participants' privacy in receiving their cholesterol numbers.

Education of Participants

Information about total blood cholesterol, HDL-cholesterol, and CHD risk provided with cholesterol measurements can improve knowledge, attitudes, and health behaviors. Effective education requires knowledgeable, trained staff supported by print (and possibly video) materials suitable for the target audience. The staff should be able to provide intelligent answers to questions about the relation of both total cholesterol and HDL-cholesterol to CHD risk. This would extend to a meaningful knowledge about the role of diet and exercise in control of total and HDL-cholesterol levels. Background information supplied to patients should be consistent with ATP II guidelines and should not embrace extremes of dietary and exercise advice that some people have advocated.

Receipt of a total cholesterol (and HDL-cholesterol) number by a participant is not sufficient in a screening program. Screenees should be able to obtain verbal and printed information on blood cholesterol from screening center staff. It is essential for public screening programs to provide education for all screenees who attend, regardless of their personal cholesterol level.

Education Recommendations

To ensure the usefulness of the screening experience, educational materials should provide:

- Information on the relationship of total blood cholesterol (and HDL-cholesterol) and other risk factors for CHD.
- Explanations on the meaning and limitations of a single total blood cholesterol (and HDL-cholesterol) value, the causes of variability, and the need for multiple measurements to define an individual as having high blood cholesterol.
- Information on the relationship of diet to blood cholesterol and the importance of a balanced healthy eating pattern to lower blood cholesterol. This should include clear information on cholesterol-lowering dietary alternatives.
- Information on the importance of following advice to seek physician followup for confirmatory cholesterol testing. Physician evaluation is especially urgent for patients with established CHD or other atherosclerotic diseases.
- Information presented by a variety of means, including print and video materials. However,

the participant should always receive print materials that delineate these messages. They should be presented in a clear and understandable format. The needs of special groups should be taken into account.

Staff Training

Staff members at public screening centers should have training appropriate to their responsibilities. Although health professionals are not required for many screening tasks, in their absence those employed should undergo training programs. These training programs and materials may come from a variety of sources; however, they should be taught by health professionals with experience in the measurement, detection, and management of high blood cholesterol.

Training Recommendations

General Training

All staff members must be made aware of the following requirements in screening programs:

- Importance of professional appearance and conduct.
- Understanding of the confidential nature of personal health information.
- Ability to deal with emergency situations such as fainting and anxiety reactions.
- Understanding of the importance of accurate information reporting and documentation of screening center activity.

Phlebotomists (Blood Drawers)

- Because errors in measurement frequently originate in poor sampling methods, technicians who collect blood should be properly trained and certified. They should have a clear understanding of sample collection methodology and the various factors that can affect cholesterol measurement such as posture, prolonged application of the tourniquet, and others.
- Technicians should understand safe techniques for infection control and prevention. This should include education on the CDC recommendations for preventing the transmission of hepatitis and human immunodeficiency virus (HIV) in health-care settings.
- Technicians should be specifically trained in dealing with participants who faint, bleed excessively, or develop other medical emergencies common to screening activities.
- Special attention should be given to hygienic aspects of the screening setting. The area of screening should be kept spotless and devoid of spilled blood; all used gloves should be immediately disposed of and out of sight.

Instrument Operators

- These operators may differ in background (e.g., nurses, technicians), but all must be appropriately trained and by CLIA requirements must have a minimum of a high school education. A minimum of 1 day's training conducted by experienced laboratory trainers should consist of classroom instruction and hands-on experience in calibrating and operating the instrument, detecting problems, and performing usual maintenance.
- Operators should have a minimum of 1 week's supervised field experience operating the instrument for cholesterol analysis before operating the instrument alone.

Staff Providing Education Information

- Screening center staff members who provide information to participants should receive training in the delivery of accurate educational messages. This should include teaching skills for clear, credible, and persuasive educational counseling. A minimum of $1\frac{1}{2}$ days should be devoted to educational counselor training. It is recognized that in-depth counseling cannot be expected in the screening setting; however, a simplified, clear message as well as factual answers to questions should be provided.

- The staff members should be thoroughly familiar with ATP II.

Screening Environment

Overall planning of the screening environment is important. Understanding of the community, its resources, and liaison with its health-care agencies are critical initial steps. These are especially important for enhancing recruitment, participation, and compliance with referral recommendations.

The physical environment of screening is important. Well-planned patterns for smoothly handling the flow of participants leave them with good impressions of the screening experience and lead to improved measurement quality. The numbers of staff and instruments should be appropriate to the expected flow rates. It is best to have a facility that allows privacy for screenees for both blood sampling and confidential counseling about the results. Laboratory technicians also work more effectively and are best able to adhere to quality-control procedures in such privacy.

Although it is not the purpose of this document to define comprehensively the organization and operation of public screening programs, certain elements are important.

Environment Recommendations

Screening programs need to make provisions for the following environmental considerations:

- The selection of settings that are conducive to handling the flow of participants, privacy during blood sampling, confidentiality of results, and discussions between participants and staff.
- Adequate staffing and equipment to anticipate expected respondent flow rates and to minimize the likelihood of the stressed, hurried environment that is associated with poor quality.
- A manual of operations that documents all procedures, including laboratory methods, within the screening center.
- Documentation of participants' results, quality-control procedures, and other relevant information in logbooks that are available for review.

Referral and Followup

A major purpose of cholesterol screening is to assist in the detection of people at high risk for CHD on account of high blood cholesterol and other CHD risk factors. The NCEP recommends that all adults 20 years of age and older should have their total and HDL-cholesterol checked at least once every 5 years. For initial testing to be complete, an accurate measurement of both total cholesterol and HDL-cholesterol is needed. However, if the HDL-cholesterol is not available, the total cholesterol level is still useful.

The effect of screening, education, and referral programs on blood cholesterol levels of populations is being studied in several research programs. In these few studies, individuals with elevated levels of blood cholesterol who complied with referral advice had significantly lower cholesterol levels on followup, and this effect remains after taking into account the statistical phenomenon of regression to the mean. Populations that receive general education on cholesterol in community health promotion programs also show a modest lowering of blood cholesterol levels at followup. This lowering appears to occur throughout the entire population range of cholesterol values and is not limited to individuals with high blood cholesterol levels. These early results suggest that public screening, counseling, and referral can lead to lower cholesterol in those who have elevated levels and to a reduction in cholesterol in populations.

One of the major goals of screening is to identify high-risk individuals for subsequent medical management. These screening guidelines recommend that the ATP II advice be followed for referral recommendations. Other considerations also are recommended below to make that referral advice effective. Before cholesterol testing, the person should fill out the risk factor questionnaire

(Appendix 1). If any of the conditions under #1 are checked, indicating the presence of atherosclerotic disease, the person should be referred to a physician. Cholesterol testing should not be used as part of the decision making in referral of such an individual. In fact, a relatively low cholesterol in such a person may give a false sense of security, and in patients with established CHD or other atherosclerotic disease, cholesterol screening should be deferred for physician evaluation. Persons with established atherosclerotic disease as outlined under #1 require lipoprotein analysis and, in all probability, specific cholesterol-lowering therapy. The answers to the questions posed under #2 may be useful in referral if the person has a borderline-high total cholesterol level (200 to 239 mg/dL). The following outlines what is acceptable and appropriate advice to give to adults undergoing cholesterol screening outside the medical setting.

1. **Total cholesterol of 240 mg/dL or higher.** Any person found to have a total cholesterol $\geq$240 mg/dL should be referred to a physician within 2 months for further evaluation and lipoprotein analysis. This referral should be made regardless of the presence or absence of other risk factors.
2. **HDL-cholesterol less than 35 mg/dL.** A person found to have an HDL-cholesterol level less than 35 mg/dL should be referred to a physician within 2 months for further lipoprotein analysis. The presence or absence of other risk factors or the level of total cholesterol does not affect the decision to refer.
3. **Total cholesterol between 200 and 239 mg/dL.** Determine the number of risk factors from question #2 of the risk factor questionnaire. Risk factors include current cigarette smoking, hypertension (or on drug treatment for hypertension), diabetes, family history of premature CHD, and age $\geq$45 years for a male or $\geq$55 years for a female. If HDL-cholesterol is available, add an additional risk factor if HDL-cholesterol is $<$35 mg/dL and subtract one risk factor if HDL-cholesterol is $\geq$60 mg/dL.
   a. If the person has two or more CHD risk factors, refer to medical care within 2 months.
   b. If the total cholesterol is between 200 and 239 mg/dL and less than two risk factors are present, it is still prudent to advise the patient to have further cholesterol testing in the medical setting. NCEP recommends repeating total cholesterol within 1 to 2 years for individuals in this category. An earlier repeat measurement by a physician within 1 year seems appropriate when the first value is obtained through screening. This is particularly the case if the HDL-cholesterol value is not available. In the meantime, the opportunity should be taken to reinforce nutrition and physical activity education.
4. **Total cholesterol below 200 mg/dL.** If an accurate HDL-cholesterol measurement is available, it should accompany the total cholesterol measurement. If an HDL-cholesterol test is not available, the person should be informed of the importance of an HDL-cholesterol measurement to complete the initial assessment of CHD risk. If the HDL-cholesterol level is available and is 35 mg/dL or higher, and the total cholesterol level is desirable (less than 200 mg/dL), the person can be advised of the potential benefit to be derived from healthy eating patterns, weight reduction (if the person is overweight), and regular physical activity. The importance of a regular cholesterol check (every 5 years) should be stressed, and it should be pointed out that cholesterol screening is not a substitute for regular medical care.

A concern about public screening is that a substantial proportion of screenees who have high blood cholesterol levels may not seek physician followup or may not heed the advice given them by a physician. This is an issue of considerable importance that should continue as a priority of screening programs and the health-care community.

In well-managed screening programs that emphasized compliance and education, as many as one-

half to two-thirds of individuals identified as having high blood cholesterol (greater than or equal to 240 mg/dL) sought advice from physicians. Specific strategies such as followup letters and telephone calls increased compliance with referral advice even more and suggested that, on average, such strategies can improve the rate of followup physician visits by 10 to 15 percent. Another approach is to mail a letter containing cholesterol results directly to the individual's physician. This approach has the advantage that it provides a direct link between the screening process and the clinical management of patients with cholesterol disorders. If the patient does not have a physician, the screening procedure can be used as an impetus to have the patient be checked periodically by a physician for CHD risk factors.

According to followup self-reports from referred high-risk individuals who visited a doctor, most were receiving appropriate attention. The majority had their cholesterol level rechecked in the physician's office.

Referral Recommendations

- Maintain liaison with sources of health care, including hospitals, clinics, and public health agencies. These provide resources for consultation and development of mechanisms for referral.
- The referral levels mentioned above should be used.
- Screening centers should have available lists of community resources that can give additional health information.
- Methods should be developed so that the majority of screenees with elevated cholesterol seek referral and medical care. Screening programs should utilize methods such as mail followup, telephone calls, or other approaches to ensure that referral advice is taken. A minimum goal is that 50 percent of referred participants are seen by their physicians within a 2-month period.

Other Issues

Cholesterol Testing in Children and Adolescents

The NCEP Expert Panel on Blood Cholesterol Levels in Children and Adolescents, in its 1991 report, noted that blood cholesterol levels of childhood tend to reflect those of adulthood, but the association is imperfect. To identify children whose elevated cholesterol levels are likely to be clinically significant, the panel recommended selective screening, in the context of continuing health care, of children and adolescents likely to become adults with high blood cholesterol levels and increased risk for CHD, i.e., those with a family history of premature cardiovascular disease or with a parent who has been found to have high blood cholesterol ($\geq$240 mg/dL). The panel did not recommend universal screening of children and adolescents or cholesterol testing outside the health care setting.

Home Testing

Devices are being developed for personal (self-testing) screening and monitoring of cholesterol levels. One of these has been recently approved by the Food and Drug Administration (FDA) for home use without prescription. There is little information regarding the utility of these devices for screening cholesterol levels in the field; their acceptability, precision, and accuracy in the hands of their intended users; and the consequences of their use. Until more information is obtained about their value and potential utility, they cannot be recommended for the purpose of screening.

Direct LDL-Cholesterol

After measurement of total and HDL-cholesterol, LDL-cholesterol is the primary decision parameter for treatment and followup. Convenient methods for directly measuring LDL and suitable for the screening environment are expected to become

available in the near future. Such methods would offer the possibility of measuring LDL- and HDL-cholesterol as an alternative to measuring total cholesterol.

Currently most routine clinical laboratories estimate LDL-cholesterol by the Friedewald equation, after measurement of total and HDL-cholesterol and triglycerides. Concerns about the reliability of the estimation have led to a recommendation for the development of direct LDL methods, using a pretreatment step to remove other lipoproteins with quantitation of the LDL by cholesterol measurement. Researchers and the diagnostics industry have responded by developing direct LDL methods. For example, the most common commercial method that is FDA-approved and compatible as a pretreatment step with a variety of analytical systems employs immunochemical separation. A mixture of antibodies specific to epitopes on the apolipoproteins of very low density lipoprotein (VLDL) and HDL is immobilized on latex beads. The specimen is added to the beads in a microfiltration device, and it is mixed and subjected to centrifugation. VLDL and HDL are retained by the filter, whereas LDL passes through and is quantitated by assaying cholesterol in the filtrates. This method is becoming common in routine clinical laboratories. In the future, similar techniques will likely be adapted to the compact analyzers used in onsite cholesterol screening programs.

APPENDIX 1
RISK FACTOR QUESTIONNAIRE

1. Have you ever had any of the following conditions?

(Check if yes)

_____ A. Been told by a doctor that you have coronary heart disease?

_____ B. Heart attack (myocardial infarction)

_____ C. Angina pectoris (chest pain due to insufficient blood flow to the heart)

_____ D. Coronary bypass surgery

_____ E. Coronary angioplasty (coronary "balloon" procedure)

_____ F. Abdominal aortic aneurysm

_____ G. Blockage of arteries to the legs

_____ H. Transient ischemic attacks (TIAs; transitory strokes)

_____ I. Blockage of a carotid artery

2. Which of the following pertain to you?

(Check if yes)

_____ A. Current cigarette smoker

_____ B. History of high blood pressure (or taking blood pressure medication)

_____ C. History of diabetes (high blood sugar)

_____ D. Heart attack in first-degree relative (mother, father, sisters, brothers, children)—if a male relative before age 55 or female relative before age 65

_____ E. Male 45 years or over

_____ F. Female 55 years or over