

NIH GUIDE

for GRANTS and CONTRACTS

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Vol. 4, No. 13, December 24, 1975

REQUEST FOR RESEARCH GRANT APPLICATIONS: RFA A N N O U N C E M E N T

TITLE: *HIGH BLOOD PRESSURE IN THE YOUNG:
EPIDEMIOLOGICAL INVESTIGATIONS OF THE PRECURSORS OF HYPERTENSION*

The Division of Heart and Vascular Diseases of the National Heart and Lung Institute is inviting research grant applications for epidemiological investigations of high blood pressure in young persons and possible early precursors of adult hypertension.

This type of solicitation (the RFA) is utilized when the Division wishes to stimulate investigator interest in a particular research area that is important to the National Program. Unlike the RFP (Request for Contract Proposals), the RFA identifies the scope of the Division's interest but does not require that proposals conform to narrowly specified research requirements or methodology. The RFA is supported through the customary NIH grant-in-aid, but it will differ from other research grants both in its goal orientation and in the degree of direct participation by professional staff of the National Heart and Lung Institute. While it is expected that each successful applicant will plan, direct, and execute his own research program, the program and any substantial modifications in it must be mutually agreed upon by the participant and the National Heart and Lung Institute. Ongoing evaluation may include periodic visits and the review of formal progress reports.

The present program announcement is for a single competition with a specified deadline (March 1, 1976) for receipt of applications. Applications should be prepared in accordance with the aims and requirements which are described in the following sections.

I. PROGRAM SPECIFICATIONS

The Epidemiology Branch, DHVD
Program Objectives
Research Scope
Mechanism of Support

II. METHOD AND CRITERIA FOR REVIEW

Review Procedures
Review Criteria

The GUIDE is published at irregular intervals to provide policy and administrative information to individuals and organizations who need to be kept informed of requirements and changes in grants and contracts activities administered by the National Institutes of Health.

Supplements, printed on yellow paper, are published by the respective awarding units concerning new projects, solicitations of sources, and requests for proposals.

III. METHOD OF APPLYING

Letter of Intent
Application Format
Application Procedure

If you have questions relating to this announcement, you should contact Dr. Manning Feinleib at (301) 496-2327.

HIGH BLOOD PRESSURE IN THE YOUNG:
EPIDEMIOLOGICAL INVESTIGATIONS OF THE PRECURSORS OF HYPERTENSION

I. PROGRAM SPECIFICATIONS

A. The Epidemiology Branch, DHVD, NHLI

The Epidemiology Branch of the Division of Heart and Vascular Diseases, NHLI, sponsors research grants and contracts related to epidemiological studies of the distribution, origins and natural history of cardiovascular diseases and their suspected etiological factors. This request for applications is intended to encourage submission of epidemiological research grant proposals designed to study precursor factors for high blood pressure in defined groups of young persons.

B. Program Objectives

Elevated blood pressure has been clearly identified as a major risk factor for coronary heart disease, stroke, and congestive heart failure in adults. In view of this, major national and local programs have been launched to educate both the lay public and health professionals about the hazards of untreated hypertension, and community screening surveys are helping to identify those individuals with undiagnosed or inadequately controlled hypertension. Large-scale clinical trials are underway to assess the efficacy and safety of treatment of mild and moderate hypertension. However, relatively little is being done to identify the precursors of high blood pressure, especially those precursors that may operate or be recognizable in young persons. Many investigators are now emphasizing that adult hypertension may have its origins in adolescence or even in childhood or infancy. The objective of the present program is to encourage epidemiologic studies which will help to identify such precursors and possibly lead to methods which may be effective in the prevention of adult hypertension.

It would also be important to study the extent to which suspected precursors in young persons can explain why certain subgroups (e.g., Blacks) have relatively higher rates of hypertension, and whether similar factors might also be important in subgroups which have not been as adequately studied (e.g., Spanish-Americans).

Active research programs are currently underway dealing with studies of renal vasoconstrictive and vasodilatory mechanisms in the adult and it is not the intent of the present announcement to support

further studies in these areas. Rather, this program would emphasize studies of non-invasive correlates of blood pressure particularly in contrasting populations defined by race or ethnic background, dietary habits, economic status, social patterns, geographic areas or other characteristics of possible importance. To the extent that biochemical and special studies are employed in the investigations, it would be expected that careful attention be paid to ensuring adequate quality control and documentation of the validity, precision and clinical significance of these studies. Although studies aimed primarily at defining the distribution of blood pressures or the prevalence of hypertension are not excluded from consideration, they will be considered to be of relatively low priority.

C. Research Scope

Some examples of the questions which may be addressed by investigations responsive to this RFA are given below. The research topics which are described in broad terms below are not intended to suggest scientific priorities but are given only to provide a perspective of the scope of research that would meet the goals of this program. Investigators are encouraged to consider other approaches and scientific questions. The emphasis of the application, however, must be directly related to elucidating the epidemiology of high blood pressure in young persons.

1. What physiologic measures or personal characteristics identifiable in childhood or adolescence are related to increased risk of hypertension?

Several physiologic measures and personal characteristics have been found to correlate with casual blood pressures measured in young persons. Among the factors hypothesized to be related to blood pressure are electrolyte intake and excretion, growth patterns and sexual maturation, obesity, heart rate and hemodynamic patterns, physical activity, and psychological and behavioral characteristics. Such correlations have usually not been adequately replicated in representative population samples nor have there been adequate longitudinal studies of these relations. It would appear desirable to test such relationships in well-designed cross-sectional and case-control studies and also in short-term (two to three years) longitudinal studies covering various population subgroups.

2. Are there specific dietary factors which are related to changes in developing blood pressure patterns?

There has been considerable speculation about the role of diet in determining blood pressure levels of individuals and also in explaining differences between various cultural and geographic subgroups. The role of salt intake, particularly in baby foods, has received considerable notice but there is still much controversy about its importance. Likewise, the effects of early infant

feeding practices are not well documented, nor are those of adolescent eating habits on the distributions of blood pressure at that age.

3. To what extent do cultural patterns, stress, urbanization and similar factors account for differences in blood pressure distribution among children in various subgroups of the population?

Psycho-social factors have frequently been mentioned as playing a role in the development of hypertension. Clearly this is an area of considerable controversy. Methods for measuring specific aspects of "stress", urbanization" and cultural patterns which may be related to blood pressure patterns are in rudimentary stages of development. Although some work has been done in adults, there is virtually no information available concerning the role of these factors among children.

4. What are the sequelae of adolescent hypertension?

The clinical consequences of fixed hypertension developing in young persons are not well documented in the literature. Although long-term prospective studies are beyond the scope of the present program, it is possible that some investigators may have access to carefully documented retrospective data that may be useful for prognostic studies. These might include high quality school records, data from pediatric clinics, other data on populations measured at early age with a high rate of follow-up. It is expected that such data, where available, would be used in complete conformity to existing regulations concerning confidentiality and privacy. Related to the problems of clinical sequelae of hypertension are the problems of appropriate diagnosis of primary and secondary forms of hypertension, definition of what constitutes hypertension in youngsters, the relation of labile blood pressure to subsequent fixed elevations, and the relation between systolic elevation and diastolic hypertension.

5. Studies of the children of hypertensive parents.

There has been much work on familial correlations of blood pressure, mostly indicating appreciable familial clustering. Little is known, however, about the age at which such clustering becomes manifest and whether it is mediated through environmental factors or is primarily genetic. To the extent that children of hypertensive parents are apt to develop elevated blood pressure during youth, it may be desirable to study trends in blood pressures among such children in relation to other characteristics as well. A more specific question which seems to have been inadequately studied is the pattern of blood pressure trends in children of women who developed toxemia during the relevant pregnancy.

The topics cited above are examples presented for illustrative purposes only; other approaches to meet the goals of this program are encouraged. Each research application should clearly define the rationale, background, specific scientific goals and detailed methods of procedure for the proposed project, including plans for the acquisition, statistical analysis, and interpretation of data.

D. Mechanism of Support

Although the support mechanism for this program will be the grant-in-aid, it will differ from the usual research grants both in its goal orientation and in the degree of direct participation by the National Heart and Lung Institute. While it is expected that each successful applicant will plan, direct and execute his own research program, the program and any substantial modifications in it must be mutually agreed upon by the participant and the National Heart and Lung Institute. Ongoing evaluation may include periodic visits and the review of formal progress reports.

Although this program is included and provided for in the financial plans for Fiscal Year 1976, award of grants pursuant to this request for grant applications is contingent upon ultimate receipt of appropriate funds for this purpose. A variety of approaches would represent valid responses to this announcement; accordingly, it is anticipated that there will be a range of costs among individual grants awarded. Applicants are requested to furnish their own estimates of the time required to achieve the objectives of the proposed research project; however, the total project period of this proposal must not exceed five years. At the end of the project period, renewal proposals for further investigations may be submitted for competitive review.

Unless stated to the contrary, the regulations (Code of Federal Regulations, Title 42, Part 52 and, as applicable to State and local governments, Title 45, Part 74) and the current policies which govern the research grant programs of the NIH will prevail.

II. METHOD AND CRITERIA FOR REVIEW

A. Review Procedures

Proposals will be reviewed on a nationwide basis in competition with each other. Primary review will be conducted by a technical review group composed primarily of non-Federal consultants; secondary review will be by the National Heart and Lung Advisory Council. Results of the competition will be announced on or about June 30, 1976.

B. Review Criteria

The factors considered in evaluating each application will be:

- o The significance of the specific objectives of the proposed project to the goals of the program as described in this announcement.
- o The scientific merit of the research design, approaches and methodology including sampling procedures, sample size, and the suitability of the sample for intra- and inter-group comparisons.
- o Evidence of cooperation from the young persons to be studied, including necessary approvals from parents and others responsible for facilitating the accomplishment of the proposed studies.
- o The research experience, and competence of the staff to carry out the proposed investigations, including expertise in hypertension research, epidemiology, biostatistics and in other disciplines that the study may require.
- o Adequacy of time (effort) to be devoted to the project by investigators and technical staff.
- o The adequacy of existing and proposed facilities and resources.
- o The adequacy of the organizational arrangements for scientific direction.
- o The evidence of institutional commitment to the program.
- o The costs in relation to the scope of the project.
- o Willingness to work cooperatively with other participants in the program.

III. METHOD OF APPLYING

A. Letter of Intent

Prospective applicants should submit a brief, one-paragraph letter not later than January 15, 1976, to:

Dr. Manning Feinleib
Chief, Epidemiology Branch
Division of Heart and Vascular Diseases
National Heart and Lung Institute
Room C-825, Landow Building
Bethesda, Maryland 20014

The Institute requests such letters only to provide an indication of the number and the scope of applications which will require scientific review. A letter of intent is not binding, and it will not enter into the review of any proposal subsequently submitted.

B. Format for Applications

Applications should be submitted on Form NIH-398, the application form for the traditional research grant. The conventional presentation for

research grant applications should be utilized; the points identified under the Review Criteria must be fulfilled. Specific attention is directed toward the inclusion of a statement indicating the willingness of the applicant to work cooperatively with other participants in the program and with the National Heart and Lung Institute.

C. Application Procedure

The receipt date for applications is before 5:00 p.m. Eastern time on March 1, 1976. The original and twenty-four (24) copies of the application should be sent or delivered to:

Division of Research Grants
National Institutes of Health
Room 240, Westwood Building
Bethesda, Maryland 20016

A brief covering letter should accompany the application indicating that it is in response to this Program Announcement - NHLI Program on High Blood Pressure in The Young: Epidemiological Investigations of The Precursors of Hypertension. A copy of the covering letter should be sent to the Associate Director for Review, Division of Extramural Affairs, National Heart and Lung Institute, Room 554, Westwood Building, Bethesda, Maryland 20016, to indicate that the application has been submitted.