



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

PUBLIC HEALTH SERVICE

BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH
Tel: 656-4000

April 6, 1964

In reply refer to:
AP 00371-01

Dr. Robert Kehoe
Kettering Laboratory
for Applied Physiology
University of Cincinnati
Cincinnati, Ohio

Dear Dr. Kehoe:

The enclosed research grant application has been assigned to the Human Ecology Study Section for scientific review. The evaluation of this proposal will be based primarily upon the following considerations:

1. The apparent scientific merit of the project, particularly in relation to other current research;
2. The adequacy of the methods and materials proposed;
3. The qualifications of the applicants;
4. The adequacy of the facilities and the research environment.

We should like to have your comments on the above points and on any other aspects of the proposal that you consider pertinent.

We would appreciate having your comments typed on the enclosed form and returned to us in order to be duplicated and distributed prior to our Study Section meeting. Since the application, like your reply, is confidential, it should be returned with your comments in the enclosed prepaid and addressed envelope. *

Please accept my thanks, and those of the Study Section, for your assistance with this review.

Sincerely yours,

Evelyn H. Halpin

Evelyn H. Halpin, Ph.D.
Executive Secretary
Human Ecology Study Section
Division of Research Grants

Enclosures

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*A reply by April 20 would be appreciated so that we may forward your comments for the information of Study Section members.

OUTSIDE OPINION
from
Dr. Robert A. Kehoe
University of Cincinnati

"Relation Between Air Pollution and Lead Poisoning"

1. SCIENTIFIC MERIT:

The primary design of the experimental program presented herein is based upon a fallacy, which the work of the authors should have recognized through their own observations as recorded in their attached report. It has been established clearly in several urban centers in the U.S.A. that lead poisoning among children results, in the overwhelming proportion of cases from the ingestion of lead compounds, principally those represented in paint obtained by exploring children, from disintegrating surfaces within neglected homes. (There are exceptions, of course.) That cases of poisoning may occur through the inhalation of lead compounds in the atmosphere of the household, has been found in a number of cities, including Chicago (as referred to in this application) from the use of battery boxes, as fuel. Present evidence indicates that the lead content of the ambient atmosphere of apparently characteristic American cities is incapable of causing lead poisoning in children or adults. If Chicago is an exception to this, even in limited (industrial) areas, it would be a surprising fact which would be worthy of detailed investigation (this might be the case, despite the available data), were it not for the apparent fact, suggested by the data submitted by the authors of this proposal, that the concentration of lead in investigated areas of Chicago is of the order of that of cities that have been investigated systematically. Moreover, the further evidence submitted, as to the levels of the concentration of lead in the urine and, more importantly, the blood of children in the suspected areas of Chicago, indicates clearly, in so far as the results can be regarded, as valid, that these children have not absorbed abnormal quantities of lead from any source. (Incidentally the equivalent of the documentary evidence submitted with this application has been denied publication because the discussion within it is flatly contradicted by the data submitted.) This bears on part #3 of this "Outside Opinion" but is pertinent here.

The etiology of lead poisoning among children, generally, in American cities is known. Certain features of its epidemiology should, indeed, be investigated, specifically (a) the basic factor (or factors) that are responsible for its seasonal character, and (b) the significance of time (the duration of exposure, whether prolonged or brief) and dosage, taken together, on the frequency of occurrence of encephalopathy (which is the lethal form of the disease as seen with unusual frequency in children). These matters require investigation of the home environment of children, and intensive study of potential, incipient and severe cases. The ambient air is, very largely if not wholly, irrelevant to the basic problem of lead poisoning in young children up to the age of 3.5 to 5 years of age. The

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principal investigator should know this, and since he does not, he has not familiarized himself or digested the information on this subject which is now available.

One has reason to be interested in the lead content of the atmosphere of Chicago (the statements (or implications) concerning the blast-furnaces of the steel manufacturing company referred to in the report attached to this application were examined by others and found to be ill-founded, but it may well be that there are some problems of this type in the industrial areas of Chicago). However, this has little or nothing to do with the immediately important problem of public health involved in the unduly high incidence of childhood plumbism.

On this account, if no other (and there is another), this proposal is made up of two irrelevant parts, and it should not be prosecuted on the remote hypothesis that the two might be found to be causally related. They should at least be dissociated, and prosecuted separately. As indicated previously, the primary environmental factor in lead poisoning in children should be the site of investigation.

2. ADEQUACY OF METHODS AND MATERIALS:

The prior discussion touches upon the adequacy of the methods, materials and scientific personnel. It may be that the specific methods of sampling and investigating the atmospheric environment and the children in the environment, for the purposes described, are intrinsically satisfactory, so far as they go. The procedures with respect to the determination of the lead content of the air may be satisfactory. Likewise the methods of analysis of the blood and urine of the children for lead (which is the most exacting of the procedures recommended for employment) may be adequate. The data thus far obtained in both of these matters are comparable to those obtained elsewhere, and this fact suggests that they are reasonably satisfactory. One has some difficulty in viewing these data without bias, however, in view of the failure of the investigators to realize their meaning. In the face of specific analytical data that demonstrate the lack of anything unusual in either the environment or the children (as a group), the principal investigator, on the basis of utterly non-specific evidence (coproporphyrinuria), decides that an appreciable proportion of the children absorbed abnormal quantities of lead. Thus the methods in themselves seem to be somewhat irrelevant. This is not a technician's quest, but one requiring scientific critique.

3. QUALIFICATIONS OF THE APPLICANTS:

This is a regrettable situation. The principal investigator is a sensitive and sincere man with instincts of a responsible physician (or so he seems, on personal acquaintance, to be). He seems utterly incapable of scientific objectivity, in the presence of the sad facts about lead poisoning among children, so that he ignores the evidence of his own data, and embarks on an experimental program in the spirit of a crusader, which has no likelihood of establishing any facts that are relevant to the experimental hypothesis. Although it is likely that useful information can be and will be so obtained, this, in the view of this consultant, is an unduly costly means of obtaining facts which will have to be sifted out of ambiguous relationships. A fully competent co-investigator, could, if permitted,

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direct this investigation into highly productive channels. In its present form and with its present guidance, it can hardly fail to confuse the issues under investigation.

RAK:vr

Robert A. Kehoe, M.D.

Date: April 13, 1964

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