

File as:

Keller J.M.

Criticism of Proposed paper on
lead & pregnancy

Letters by G.J. Steggs

Paper not available

N36893



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WILMINGTON, DELAWARE 19898

EMPLOYEE RELATIONS DEPARTMENT

HASKELL LABORATORY
FOR
TOXICOLOGY AND INDUSTRIAL MEDICINE

July 23, 1970

J. M. Keller, M. D.
Dept. of Obstetrics and Gynecology
University of Illinois
Medical Center
840 South Wood Street
Chicago, Illinois 60680

Dear Dr. Keller:

I received the manuscript of your paper "Blood Lead in Pregnant Women and Neonates" to review and felt that because of our special relationship with regard to this paper, since the Du Pont Company had financially supported it, and the analyses had been performed in our laboratories, that I should write to you directly concerning the publication of this paper.

I feel very strongly that in its present form the paper requires considerable revision and would offer the following suggestions. As set out in the abstract the purpose of the paper is said to be "to evaluate whether the increase in atmospheric pollution by lead increased the blood lead content of 410 pregnant females and 104 newborn infants. To answer this question only two maximum blood lead values are given, one for patients having urban addresses and one for patients having rural addresses. To provide a satisfactory answer to this question at least the means and standard deviations for the two groups should be calculated and any difference in means tested by accepted statistical techniques for significance. If a significant difference is found, one possible explanation for the difference would be the air lead concentration to which the groups were exposed but other possible explanations such as differences in diet would have to be discussed and the actual air concentrations of lead in the area of the study measured or estimated. It is noted in the paper that comparisons were made of the influence of other factors than place of residence, such as stage of gestation, season of the year and sex of the infant, but none of this potentially very interesting data is offered in numerical form.

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It is stated that the lead level was somewhat higher in term pregnancies, but there is no discussion of the problems of accurately measuring the lead levels in the blood of women with a changing fluid balance and red cell mass during gestation.

In the preamble, reference is made to Nogaki's paper which claims an increased risk of abortion with blood leads exceeding 40 micrograms of lead per 100 grams of blood. It would seem to me that again a single figure is not sufficient information and that one needs to know the mean blood lead as well as the range of values for the group, but that since you have introduced the subject of abortion some reference to the outcome of the pregnancies in your study should be made. Were there abortions, stillbirths, neonatal deaths or fetal deformities? If so, these should be documented and their statistical significance assessed.

In conclusion your reference to the "normal blood lead level" raises the problem that to many persons lead poisoning can be diagnosed solely from a blood lead level, whereas lead poisoning is a clinical diagnosis to which knowledge of the blood lead level can make a significant and useful contribution. "Normal" in the sense used here and in your paper means "commonly found" and being outside the normal range is not necessarily the same as suffering from lead poisoning.

I hope these suggestions will be of value to you. It seems to me that this study and others that we conducted at the University of Pennsylvania pointed to the complexities of carrying out longitudinal studies of lead levels in pregnant women and perhaps formed pilot studies for a more definitive piece of research. Probably the only clear conclusion that can be drawn from the original data is that lead crosses the placental barrier to give essentially the same blood lead level in the fetus as in the mother.

Sincerely,

ORIGINAL SIGNED BY
JOHN A. ZAPP, JR.

G. J. Stopps, M.B., B.S.
Assistant Director

GJS/rjm



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July 22, 1970

Robert A. Kehoe, M.D.
University of Cincinnati
Department of Environmental Health
Kettering Laboratory
College of Medicine
Eden and Bethesda Aves.
Cincinnati, Ohio 45219

Dear Bob:

I have just returned from four weeks of vacation to find your letter and the Keller manuscript on my desk. The paper arises from some preliminary studies which we sponsored some years ago in trying to answer the question: "Is lead mobilized from the maternal skeleton during the period of high calcium demand by the fetus in late pregnancy?" The results of this and some other studies we carried out at the University of Pennsylvania convinced me that without a specific interest in this particular problem by the clinical group involved and a much more sophisticated experimental design than could be undertaken in the conditions usually found in the outpatient department of an obstetrical service, the question could not be answered. As I am sure you will appreciate far better than most people the relationship between the university person carrying out a piece of research and those responsible for partial or complete financial support can be a delicate one. In the case of Dr. Keller, personal relationships were always good, but it quickly became apparent to me that my original idea of how many mothers would need to be studied and the number of analytical samples required from each mother were inadequate and therefore I regarded the study by Dr. Keller purely as a pilot study and that to carry out a definitive study would require a much more sizeable effort than was feasible at that time.

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Robert A. Kehoe, M.D. (Cont'd.)
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Of course the results of the blood analyses were freely available to Dr. Keller to use if he felt a useful contribution to the scientific literature could be extracted from them. I had hoped that the lack of any publication over the intervening years reflected Dr. Keller's appreciation of the sketchy nature of the available data even if it were set out in full, but apparently this is not the case.

I am glad you have expressed yourself firmly and forcibly on the merits of the paper since a similar expression of opinion on my part might be interpreted as an attempt to suppress publication.

I am sorry that you have been bothered by this matter and hope that in giving the background to the "study" you will understand my position. With best regards.

Sincerely,

ORIGINAL SIGNED BY
JOHN A. ZAPP, JR.

G. J. Stopps, M.B., B.S.
Assistant Director

GJS/rlm