October 9, 1961

Memo to: Dr. Robert A. Kehoe

From: Dr. Theodor D. Sterling

Subject: Forthcoming Chamber Experiments

The following experimental suggestions are based on the analysis of existing data, our own developments of a physiological model, and on a series of discussions with you, Dr. Horton, and others.

A. Pre-experimental Ingestion Trials

The determination of how much of ingested lead is immediately excreted has proven to be difficult because subjects are in a state of equilibrium during their control periods. The amount of lead excreted during such an equilibrium equals (approximately) to the amount of lead ingested. Estimates of the proportion of intake that passes through the gut had to be based on variations in intake and subsequent variations in fecal excretion. These estimates have never been satisfactory. Yet the knowledge of this proportion is extremely important since the normal body burden of lead consists largely of that ingested material which is not eliminated immediately.

In addition the data of certain of the inhalation experiments has shown that a part of the inhaled lead may be swallowed and so acts as if it were ingested. Again estimates of the proportion that passes through without being absorbed into the body are useful.

Each individual subject may differ, to some extent, in the proportion so eliminated. It would be useful therefore to obtain such an estimate for each subject before a constant increment of lead is added to his environment.

The experimental paradigm for the Chamber Study or the lead ingestion experiment should be modified as follows:

Period I, Control 1: Measurement of average intake and excretion of lead are obtained. This period need not exceed 30 weeks in duration.

Period II, Control 2: Estimates of proportion of ingested lead that ~~is excreted~~ traverses the alimentary tract, unabsorbed, are obtained. The subject is given orally between 1 mg to 3 mg of lead every 7 to 10 days. A minimum of 12 such observations should be made.

Period III, Exposure: (As in previous experiments.)

Period IV, Post Experimental Control: (As in previous experiments.)

B. Experiments on Variable Intake of Lead

One important experimental question concerns itself with the effect of ongoing 24 hour long intakes from the atmosphere. To evaluate these long duration exposures to lead in the atmosphere it is necessary to study the effects of variable length of stay in the chamber. Such an experiment has been performed last year and should be repeated at least once more. The design of last year's experiment can be used with the only change introduced by the pre-experimental ingestion trials described before.

A second experiment of this type should be performed on ingested lead. The lead model draws a number of conclusions for the case where variable amounts of lead are ingested. These could be verified directly. While some data relevant to variable intake would be obtained from the suggested pre-experimental ingestion trials, an experiment on long term variable ingestion would be a valuable contribution.

C. Animal Studies

According to our discussion on testing theoretical developments on animals I would recommend the parallel undertaking of animal work. I have discussed the feasibility of such work with Dr. Horton and find that he is in agreement with me both to the advisability and feasibility of such studies. The existence of suitable lead isotope, Pb^{210}, would make such a study highly practicable. I would suggest that we meet with Dr. Horton and discuss this further.

OK

cc: Dr. Horton
Dr. Phair