

PROGRESS REPORT - PROJECT NO. LH-75

INVESTIGATION OF HUMAN EXPOSURE TO PARTICULATE LEAD COMPOUNDS IN THE AIR UNDER EXPERIMENTAL CONDITIONS

The work outlined in previous reports of progress, the last of which was dated September 10, 1964, has been directed primarily toward the determination of the maximum concentration of ideally respirable (that is, particles of lead too small to be deposited in the upper respiratory tract) inorganic lead in the atmosphere, that can be inhaled continuously throughout a lifetime by normal, healthy persons, without demonstrably progressive accumulation of lead in their bodily tissues.

The approach to this problem is patterned on the results of balance experiments (intake of lead in food and beverages, and output in the feces and urine) carried out previously with human subjects under various conditions. In the present experiment, such subjects, after preliminary observation of their lead metabolism under normal conditions, are subjected to the inhalation of air containing lead in a known concentration over periods of time sufficient to demonstrate the occurrence of non-occurrence of a physiological response in the form of an increase in the urinary output of lead. (This response can be detected before any other in the intact human organism.) It is postulated, on good grounds, that the response of human beings to continuous exposure of this type can be determined with approximate accuracy by extrapolation from the results of regular incremental increases in the duration of intermittent exposure - that is, x hours of exposure per day for a suitable time, followed by 2x, 3x and 4x hours of exposure, for comparable periods of time, will yield a series of points on a curve which can be

extended to 24 hours per day, every day.

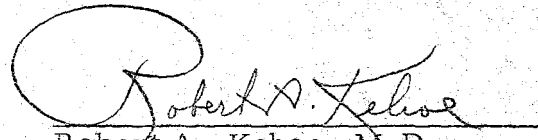
In a continuation of previous experiments, Subjects [REDACTED] and [REDACTED] in essentially parallel experiments, have been subjected to exposure to lead sesquioxide dispersed in the air of the two respiratory chambers in particles ranging from 0.01 to 0.18 micron in diameter (mean size 0.05 micron) in the concentration of approximately 10 micrograms of lead per cubic meter. (After preliminary control observations, over a period of months prior to the year 1965), these subjects were introduced into the chambers for 3 hours on every other day (10.5 hours per week) over the period of 12 weeks. Subsequently the duration of the exposure per day was doubled, trebled, and further multiplied until, at present, August 18, 1965, one of the subjects ([REDACTED]) is spending 63.0 hours per week, in the chamber, while the other ([REDACTED]), who started a bit later) is spending 52.5 hours per week, both having passed through periods of approximately 16 weeks of exposure for 10.5, 21, 31.5 and 42 hours per week, respectively, while Subject N.K. was subject to, additionally 52.5 hours per week for 16 weeks, before undergoing the present phase of the experiment.

There has been no demonstrable excretory response on the part of either subject to the experimental regimen. That is to say that the quantity of lead absorbed daily in the lungs of these subjects has not been sufficient under these conditions to be demonstrated in the face of the variability of the urinary excretion of lead from day to day induced by the absorption from the alimentary tract. Or to be still more specific, the quantities of lead absorbed from the alimentary tract from day to day are so much larger (they can be expected to be much more variable, also) than the quantities absorbed daily from the lung that the latter cannot be detected.

It is necessary to obtain a response, and in fact to obtain a series of increasing excretory responses, in order to obtain the data for extrapolation from intermittent to continuous exposure. Therefore the experiment must be continued in increasing increments of severity (concentration of lead in air and duration of exposure) until such data have been obtained.

One would wish to expedite the experimental procedure so as to obtain definitive results more promptly and at lesser cost. However, in view of the total lack of experimental precedent, and because of the risk of overshooting the mark (in terms of concentration of lead in air) and thus rendering the subjects unfit for further observations, it seems wise, at this time, to follow the original experimental design during the coming year. If this is done, and if it is necessary, as seems likely, to go beyond the level of 10 micrograms of lead per cubic meter of air in order to obtain an excretory response, the procedure will be that of beginning the new level of exposure at a point, in terms of concentration and time, which is judged to be equivalent to the next serial increment of increase in intensity. Once a response has then been obtained and stabilized (other data indicate that a plateau of response will have been reached in 16 weeks, at most), the course is set for the addition of further points in a curve which will yield the approximate value for continuous exposure. There does not appear, at this time, to be a short cut to this result, and in view of the investment of time and money in this experiment and in the metabolic evidence on which the experiment is founded, it would seem unwise, now, to alter the design. However, at the end of this year (1965), the experimental data will be reviewed critically, as a means of checking the experimental design and of affecting such reduction of time, effort and monetary expenditure as may be feasible. Such modification of procedure as may seem feasible and wise will be communicated to the sponsors for comment and criticism,

so as to achieve the maximum benefit from the collective critique. Considering the present situation of the principal investigator (on leave in the service of Pan-American Health Organization for the next three months) as well as the present stage of the experiment, it is believed that no useful purpose would be served at this time by assembling the data that would merely illustrate the negative results of the experiment as conducted up to this point. It should be emphasized, perhaps, that the very negativity of the results, in relation to the point of significance that remains to be established is an extremely important finding.


Robert A. Kehoe, M.D.
Principal Investigator

Date: August 18, 1965

KE 0004436