

PROGRESS REPORT ON PROJECT NO. LC-75

"Human Exposure to Ambient Air Concentrations of Particulate Lead"

Reference is made herein to our proposal of October 3, 1962, and to our further proposal of September 4, 1963, in which the general experimental program for the investigation of the fate of ambient, particulate lead in man, was described briefly. The latter proposal dealt specifically with the continuation of this program through the calendar year 1964. As indicated therein, the last prior experiment had been terminated, except for the completion of the analytical work. The two subjects so involved had completed their participation as subjects, as of September 8th, 1963, and the data were yet to be obtained, in full, and subjected to examination. These have since been assembled and are now being analyzed statistically and represented graphically.

The specific experiment, now in progress, as described in the proposal of September 4, 1963, was designed to employ two human subjects, who had been engaged and were under observation in 1963, from March 19th onward. The entire set of experimental observations, as indicated previously, consisted in the collection of duplicate specimens of all food and beverages consumed, on a day-by-day basis, together with the corresponding daily collection of all feces evacuated and all urine voided. Specimens of blood (in duplicate) were obtained at weekly intervals. Certain detailed physical and clinical laboratory examinations were carried out, and the results were recorded, weekly. The specimens referred to above were analyzed for lead, in accordance with standard procedures, and all of the information, including the analytical data, were recorded, transferred to punch cards for statistical purposes, and, in addition, were charted and graphed, on a weekly and monthly basis, in such a manner as to portray the

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relationships between the intake and output of lead on a moving temporal basis.

The preliminary observations on these two subjects were concluded at 8:00 A.M. on September 9th, 1963, when the subjects were scheduled to enter upon a regimen of exposure to lead in two respiratory chambers which were to be operated in parallel, under essentially identical conditions.

Unfortunately, at this time, one of the subjects (who had presented us with certain difficulties, from time to time, which were resolved successfully) became somewhat more demanding, in ways which compromised his reliability as the subject of further observations. A decision had to be made at this time whether to risk further expenditures of funds and effort, or to acknowledge that a mistake had been made in his selection. In view of the stern necessity of depending upon the absolute reliability of the experimental subject in following instructions, only one course was open, and this subject was discharged. (While the results obtained in the investigation of this subject, up to that time, are not a total loss, from the aspect of the general investigation of normal human subjects, they are worthless for the purpose of this experiment, so that the cost of this work must be regarded as an unprofitable expenditure. This is the first failure of this type encountered in the many years of such experimentation, and while it is not an altogether surprising occurrence, it is nonetheless unfortunate. The threat of a second failure arose out of our efforts to replace this subject without delay, in that a young man seeking employment was engaged promptly, (September 30, 1963) and after a careful inquiry, examination and observation, was discharged 11 days later (October 11, 1963). Not until October 22 was a suitable subject found (with the help of several interested persons), employed, and inducted into the preliminary stage of the observations.) Meanwhile, the remaining subject

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of this pair was first introduced into a respiratory chamber on October 7th, 1963, despite the necessity of his "going it alone," and the decision was made to find the other member of the pair at the earliest possible time, to abbreviate the preliminary period of observations by as much as his metabolic behavior would permit, and to get him into the other chamber for parallel observations with as little delay as might prove to be possible. The preliminary observations on the latter subject were initiated on October 22, 1963, and were terminated on March 2nd, 1964, at which time it was evident that his behavior, with respect to his intake and output of lead, was in *general* accord with the ^{*usual, previously noted,*} ~~normal~~ pattern. On this date (March 2nd), in the second respiratory chamber, he entered upon the same schedule of experimental exposure to lead as that of his fellow-subject (who, as indicated above, had entered upon this schedule on October 7th, 1963).

The Present Experiment

In order to set forth the full scope of the experiment now in progress, and to separate it out from the prior experiment, it may be helpful to restate the experimental objectives being sought in both instances.

- (a) In the first of these experiments, also carried out with two persons, subjected, as nearly as possible, to identical conditions, the concentration of lead in the respiratory chamber approximated 0.15 mg. of lead (Pb), as lead sesquioxide. The subjects were confined in their respective chambers, first for 3 hours per day on every other day, for 16 weeks; then for 6 hours per day, on every other day, for 16 weeks; then for 9 hours per day, on every other day, for 16 weeks; and finally, for 12 hours per day, on every other day, for 16 weeks. The charted results demonstrated the expected relationships. Considering

only those facts and relationships which are of primary importance, the concentration of lead in the urine and in the blood of the two subjects rose in successive steps, in response to the increases in the length of the periods of exposure, reaching practically identical levels in the urine of each subject, and also in the blood of each subject, at the successive steps, so that, at the final step, these values were, respectively, for Subject [REDACTED] 0.082 mg. of lead per liter (urine), and 0.05 mg. of lead per 100 g. (blood), and for Subject [REDACTED] 0.080 mg. of lead per liter (urine), and 0.053 mg. of lead per 100 g. (blood). An extrapolation of these findings (by the simple extension of the slope of the curve of increasing concentration to the point of intersection with the vertical line at 24 hours per day) so as to portray the effects of such exposure on every other day, showed that both of the subjects would have reached a ^{potentially?} dangerous level of absorption (as judged by the threshold level of 0.08 mg. of lead per 100 g. of whole blood), in that Subject [REDACTED], at this point in time, would ^(probably) have had 0.084 mg. of lead per 100 g. of blood, and Subject [REDACTED] would ^(probably) have had 0.082 mg. of lead per 100 g. of blood. (In as much as the experimental exposure to lead occurred on every other day, rather than every day, the level of dangerous absorption of lead would have been arrived at in about half the time (somewhat less than 1 year) had the exposure been continuous, that is for 24 hours per day, on every day. Or to state the case in the terms of the experiment, it is reasonable to conclude that, had the exposure been continuous (i.e. all day every day), at the level of 0.15 mg. of lead per cubic meter of air, the concentration of lead in the blood would have reached the level of approximately 0.16 mg. per 100 g., in somewhat less than 2 years of exposure.) It has been demonstrated clearly,

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that the respiratory exposure of normal men to highly dispersed lead sesquioxide in the atmosphere, on a schedule which is comparable to that of industrial employment (approximately 40 hours per week), will not result in a dangerous degree of absorption. The influence of discontinuity, in contrast with that of continuity, in exposure to lead, may thus be appreciated on a fairly quantitative basis.

- (b) Having demonstrated, in the preceding experiment, the influence of time, that is, the continuity of the period of exposure, the next experimental step involved the determination of the highest level of the concentration of lead in the air to which a normal individual might be subjected continuously, without incurring a measurable increase in the concentration of lead in his urine and blood (presumably, without significant increase in the "body burden" of lead). This, for practical purposes, might be regarded as the intensity of respiratory exposure which, if continuous, would just barely result in a statistically demonstrable increase in the urinary output (or concentration) of lead, without a demonstrable increase in the concentration of lead in the blood. (Prior experimental evidence has shown that such a situation results from a careful adjustment of the increment of lead added experimentally every day to the quantity absorbed from day to day under normal conditions.)

The experiment was designed in the following manner. Two experimental subjects were to be employed in identical schedules. (As pointed out previously, the failure of one of the pair to continue as a subject resulted in different timing for the two (eventual) subjects.) Subject [REDACTED] completed the preliminary observations on October 6, 1963, and entered the chamber for the first time on October 7, 1963. At this time he was subjected, for 3 hours, to the

inhalation of air containing approximately 9 micrograms of lead (the sesquioxide) per cubic meter. This regimen continued, on every other day, until January 16th, when the length of time spent within the chamber was increased to 6 hours on alternate days under the same conditions otherwise.

The second subject, [REDACTED], was engaged in the preliminary observations from October 26th, 1963 until March 2nd, 1964, when, for the first time, he entered the respiratory chamber and was subjected for 3 hours to the inhalation of air containing approximately 9.0 micrograms of lead per cubic meter. He will continue under this regimen (on alternate days) for a period of time equivalent to that spent by the first subject ([REDACTED]) under these conditions, namely 14 weeks. At the end of that time, he too will enter upon 6-hour periods of exposure to the same conditions, on every other day.

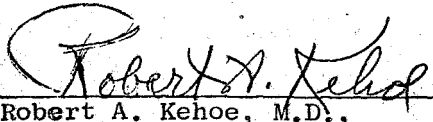
When each of the two subjects shall have completed the second step in the experiment, as described above, the duration of the period of exposure on alternate days will be increased to 9 hours, and after that, in all likelihood, to 12 hours. Then, after such period as may be necessary, if any, to restore the subjects to base-line status, the experiment will be continued at twice the concentration of lead in the chamber. It may be necessary to advance the concentration to three times that of the initial. This seems unlikely, but remains to be determined by the results of the prior experiments.

Results of These Investigations

The results obtained by the experiment which has been completed (the initial experiment described herein) have been reported verbally to the

sponsors of this program of investigation. As soon as the results of the terminal part (post-exposure) of this experiment have been charted, (the last of the materials to be analyzed were obtained on September 8, 1963, and were processed only recently), they are being subjected to statistical analysis and graphic representation, after which, as soon as possible, a formal report will be brought to completion.

The outcome of the experiment which is now under way has to be appraised at the end of each step, so as to indicate the course of successive steps. All that can be said, at present, is that the intensity and duration of the respiratory exposure of the first subject () in the first and second steps (to air containing 9 micrograms of lead per cubic meter), were not such as to furnish any demonstrable evidence of an increase in the rate of the absorption of lead. That is to say, that the degree of absorption (if any) which occurred under these conditions, in excess of that of the control period, was below the threshold of experimental detection. This, it should be said, was the expected result, for the conditions of the first and second steps were intended to be below the threshold, since it is the objective of the entire experiment to reveal this threshold.


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