

MEMO ON PROGRESS OF A.P.I. PROJECT L-6

The two subjects, Subject S.S. and Subject H.H. have continued on the experimental regimen outlined in letter of April 17, 1968, from Robert A. Kehoe to Melvin R. Plancey.

Subject S.S. will complete the last lap of his exposure on October 6, 1968, as agreed upon by him some months ago. At that time, in the present experiment, he will have been exposed to air containing 20 micrograms of lead as the sesquioxide over the following periods of time:

20 weeks at the rate of 31.5 hours per week
16 weeks at the rate of 31.5 hours per week

20 weeks at the rate of 42.0 hours per week

16 weeks at the rate of 52.5 hours per week

16 weeks at the rate of 63.0 hours per week

16 weeks at the rate of 73.5 hours per week

There is little question that in the latter part of this experiment, the rate of the Subjects' excretion of lead in the urine has increased. There seems not to have been a corresponding increase in the concentration of lead in the blood. The statistical work has not been done, and these tentative conclusions have been arrived at only by inspection of the data. This is, however, the result which has been anticipated as the result of previous experience. That is to say that the first and only physiological response to the minimum of increase in exposure to lead is that of a significant increase in the urinary lead concentration and output, without any demonstrable increase in the concentration in the blood.

This Subject is to be followed as to the lead in food and beverages and in feces, urine and blood, for a period of two or three months, following the termination of the respiratory exposure to lead, in order to determine whether or not there is a demonstrable decrease in the lead content of the urine and blood. By this means, the verification of the effects of exposure can be made doubly certain.

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Subject D.H. completed the preliminary period of the metabolic observations on July 7, 1968. He entered upon the several periods of respiratory exposure to lead on July 15, 1968. Here, again, the concentration of lead in the chamber is 20 micrograms per cubic meter. The initial length of the exposure, 48 hours per week, is now in its 12th week. The entire experiment is scheduled to continue according to the following schedule:

16 weeks at 48 hours per week, terminating on November 3, 1968

16 weeks at 60 hours per week, terminating on February 23, 1969

16 weeks at 72 hours per week, terminating on June 15, 1969

16 weeks at 84 hours per week, terminating on September 22, 1969

The exposure is to terminate at this point and a brief period (2 or 3 months, or less, if the results are clear-cut before that time, perhaps in 1 month), and a brief period of post-experimental observations will be carried out.

It is believed, on the background of the presently available information, that with this experiment, this approach will have yielded the required information in a definitive manner. It is possible, of course, that Subject D.H. will react more sharply than Subject S.S., so as to shorten the estimated time. It is also possible that he will find the schedule a bit severe, and that it will have to be adjusted. Our purpose is to make this the final experiment of this precise type and to render the conditions as severe, in terms of the time spent by Subject D.H. in the chamber, as may be feasible. Thus, it becomes a crucial experiment.

As soon after Subject S.S. has completed the present period of exposure, on October 6, and the analytical data can be completed, statistical examination of the data will be undertaken. It is thought that a preliminary estimate of the significance of the results can be reported before October 18, 1968.

April 17, 1968

Melvin R. Plancey, M.D.
Medical Director
Atlantic Richfield Company
260 South Broad Street
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Re: Project L-6

Dear Doctor Plancey:

I hasten to reply to your letter of April 11 for two reasons. One of my purposes is to clarify your view of the progress and status of the investigation in which your group is sharing as co-sponsor. The other is to offer my direct services in providing information to your group beyond that which can be passed on to you at this time in a letter. I could meet with your group on May 9th, for as long or as briefly as you wish, just for the purpose of acquainting you with the progress of the work and that which needs to be done further in order to bring it to adequate fruition. I'm afraid that Harold Golz was misled, probably through our failure to discuss the matter at length, into the belief that this entire investigation would come to an end before the end of this year. He may also have conveyed to you an incorrect concept of the nature of an experiment such as might be conducted in the prison of which he spoke. I think, therefore, that it might well be useful to deal with these matters, at least briefly, or perhaps in a preliminary manner, at your meeting.

While I would agree enthusiastically as to the desirability of a plan such as your group appears to have in mind, I feel sure that one would have to have the information from the present type of experiment, before he could proceed with the details of a continuous experiment. The latter would be a fairly crucial test of the validity of the concept involved in the more comprehensive experiments, and would, I believe, have to be relatively brief. It would not be easy to conduct, in any case, but I can conceive of conditions under which it would be feasible.

I must express my belief that the determination of the physiologic threshold level of lead in the air breathed continuously by normal healthy persons, is the most important item in this entire field of investigation. Without it, we shall not be able to derive a standard for human safety; with it, we can be secure in our position.

The present status of the work may be described as follows:

1. Two Subjects, in parallel, Subject S.S. and Subject H.R., entered upon an experimental regimen which consisted in being subjected to the scheduled inhalation of air containing 20 micrograms of lead sesquioxide, in a particulate dispersion at the mean diameter of 0.05 micron, the maximum size being approximately 0.2 micron. After the preliminary observations had been completed, to establish the levels and the patterns of the intake and output of lead by the two subjects under control conditions, their exposure within the parallel respiratory chambers was initiated on ~~February 27, 1967~~, at the temporal level of 21.0 hours per week.

October 10, 1966

This was to continue for from 16 to 20 weeks, dependent upon the results obtained, and then was to be advanced, for similar periods, to 31.5, 42, 52.5, 63, 73.5 and 84 hours per week, or until such a time as would provide a series of four progressively increasing responses to the lengthening severity (duration) of the exposure. Unfortunately for completion of this program (fortunately for Subject H.R.), word was received by him in the late Spring of 1967, that he had been awarded a graduate scholarship at Yale University which would require him to be in residence there by the end of August 1967. This wholly unexpected award was so obviously to the great advantage of this man, and to his future in his chosen field of graduate study, that we could not take any other course but that of encouraging him to follow his opportunity. This necessitated a revision of his experimental regimen at the proper time, so as to obtain the most information that could be had during his remaining time. Therefore, the severity (duration) of his exposure within the chamber was increased two stages ahead of the original schedule in order to obtain evidence, ahead of that being sought from the other subject, of an increase in his excretory response to this exposure. (By this means we could expect, subsequently, to obtain the same type of information, under the same conditions, from the other subject. Subject S.S., therefore, who would remain with us, would be kept on the original schedule, while Subject H.R. would be moved ahead.)

As soon as possible, after this situation developed, a further subject was secured, after appropriate inquiry and investigation, and started (November 6, 1967) upon the preliminary (control) observations.

As a result of these circumstances, plus the fact that Subject S.S., who is now in the fifth (63 hours per week) stage of the scheduled exposure to lead within the respiratory chamber, is to be relieved in October of 1968 of his duties as a Subject under respiratory exposure to lead, this experiment will be terminated as far as exposure to lead is concerned, in October. Hopefully, and on present appearances, we shall have obtained from him most of the information we require from him by that time. Since he is not leaving town but rather is engaging, (through a prior agreement with me), in a period of teaching and study that is incompatible with further confinement in the respiratory chamber, we can follow his progress in the intake and output of lead for a sufficient time to reveal any subsidence in his urinary lead excretion and in the lead content of his blood after the discontinuance of his exposure.

2. A new Subject, D.H., procured in November 1967, will be used in such capacity as may be required to check or confirm the results obtained in the investigation of the other two subjects, or will be introduced into a new experiment which is under contemplation at this time. We shall be prepared to consult with the sponsors of the program in their consideration of this experiment.

3. My personal and professional plans for the future come naturally to the fore in the consideration of further similar or new experiments. I do not wish at this time to make any statement in that regard, but I think it very likely, that the present year is one of decision for me, in view of a number of factors that appear to be coming to a head. I am not suggesting that I shall walk out of a relationship to the sponsors of this work, so as to leave the project incompleted and the sponsors in the lurch. What I recognize is that I must, soon, reach a

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decision as to my future professional plans. Mrs. Kehoe and I must also decide where we are to live, ultimately, and how soon we must make such change as seems desirable. I believe, therefore, that I should obtain some idea of the interests of the Sponsors of our experimental program on lead at a reasonably early date. Therefore, some informal exchange of views would, I think, be desirable. The issues here, in my opinion, are fairly clear and should be given careful consideration. Your group represents only one important segment of the sponsoring organizations, and I would be glad to know where we stand as of this time.

With kind regards,

Cordially yours,

Robert A. Kehoe, M.D.
Professor Emeritus of
Occupational Medicine

RAK:wp

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Melvin R. Plancey, M. D.
Medical Director

April 11, 1968

Robert A. Kehoe, M. D.
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Dear Bob:

At the last meeting of the Environmental Health Committee of the API, we discussed the progress of your jointly sponsored research project (our designation L-6) involving human volunteers exposed to lead in inhalation chambers. At that time Dr. Golz of the API staff reported on his conversations with you concerning the project. We were informed that there was a good possibility that it would be terminated before the end of the year. Our committee will be meeting again on May 9. I would like very much at that time to be able to give the members more definite information. Would you be kind enough to let me know precisely the status of the project?

Regards,



Melvin R. Plancey, M. D.

MRP:G

P.S. I believe that Dr. Golz may have indicated to you that we are planning to explore the possibility of twenty-four hour exposure of humans in a prison where other research proposals have already been performed.

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