

April 16, 1953

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Dear Doctor Archer:

I am very pleased to send you, under separate cover, a series of articles on the absorption and excretion of lead. The data that relate to the retention of lead, under the influence of the absorption of small quantities, is available at present only in the terms of our experiments on human subjects who ingested small quantities of lead over long periods of time. Unfortunately the full data of these experiments have never been published, for the lack of time on my part to get the information together. However, the articles will illustrate some of the matters in which you are interested. If questions come to your mind which are unanswered by the data, and if you should care to direct these to my attention, I shall be pleased to reply as fully as I can. I feel very guilty in not having published the full data of these experiments, but we have been so involved in a variety of activities, which have appeared to have come to a head within the last few years, that I have literally been swamped, and I have neglected what I consider to be my professional duties, on the experimental side, for other duties which have appeared, at least externally, to be more urgent.

I think I should point out to you that we are now engaged in a prolonged and elaborate study of the influence of the inhalation of lead on absorption and excretion. Following substantially the same techniques that we have used in our study of lead ingestion, we are undertaking to determine the total intake and output of lead on the part of subjects who spend 7 1/2 hours a day on 5 days per week in a respiratory chamber, in which they are exposed to a specific concentration of a specific compound of lead in a definite and determined state of subdivision. In the course of these experiments, over a period of years, we expect to investigate, in some detail, the influence of dose, of particle size, and of chemical compound (solubility, etc.), on the absorption of lead from the respiratory apparatus. Inevitably, along with this, when we come to use particle sizes of adequate magnitude, we shall have a great deal of separation out in the upper respiratory

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tract, and a very considerable amount of ingestion with consequent absorption of inhaled lead from the alimentary tract. This problem has never been appraised in proper relationship to its importance. It is undoubtedly one of the highly significant factors in the absorption of lead under conditions of respiratory exposure.

The first of the experiments of the type described above is virtually complete, in that an experimental subject who has been exposed for two years to finely divided lead oxide, in the concentration of 0.075 milligram per cubic meter (particle size 0.05 micron), reached an equilibrium, with respect to the maximum concentration of lead in the blood and the maximum rate of lead excretion in the urine, in approximately six months, after which time he went along on a plateau, substantially, for the balance of the period. This corresponds to the behavior of men under well established and uniform conditions of occupational exposure, and it is, therefore, a very gratifying result. In the course of this experiment, in which the respiratory retention of lead was determined at fairly frequent intervals, the individual absorbed from the respiratory apparatus approximately 50 milligrams of lead, of which approximately 30 were excreted, leaving a retained quantity of approximately 20 milligrams. These values, of course, are estimates, which could vary slightly from the true value by virtue of a certain rather small experimental error. The quantitative deviation here, however, is quite small, and thus the order of magnitude of the figures cited above is entirely correct.

I think I should point out one difficulty in the determination of the quantity of lead that is available in the body, by means of measurements of the lead in the body fluids, blood and excreta. The skeleton constitutes a reservoir, so to speak, for retained lead, and in the course of the stay of the lead in the skeleton it appears to be able to move from the point of original deposition to the more remote parts of the skeleton, as time goes on. In other words, at the time of the original deposition lead is deposited in the areas of most active metabolism, but as time goes on and as some of this is lost from the skeleton, the distribution of lead throughout the skeleton becomes substantially uniform. This means that that which is in the more remote part of the skeleton, speaking in metabolic terms, is not inert, but is much less readily metabolized than is that initially retained. Therefore, there is a lag in the determination of the relationship between lead in the skeleton and lead in the circulating medium and in the urine. Perhaps the best and simplest way of describing this situation, is to point out that the loss of lead from the body after its deposition is a function not only of the quantity deposited but of the time over which the deposition occurred. Thus if the quantity is small and if it is deposited over a long period of time, it provides a lesser head of pressure, so to speak,

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for excretion, than would a corresponding quantity absorbed and retained over a short period of time. I am in the habit of saying, as an inaccurate rule of thumb, that it takes twice as long to get rid of the lead as it does to deposit it. It is obvious, however, that it may take much longer than twice as long, when the quantity is small and when it is strung out over a long period of time. Thus in the case of the experiment described above, our subject who had retained an extra 20 milligrams of lead, at the time of the termination of the exposure, reached a substantially normal level of excretion after a period of about a month. All this means is that he so nearly reached the normal level that the difference is not recognizable from day to day in our determinations of intake and output. In other words, this might be of the order of magnitude of a hundredth of a milligram per day, in which case it is too small to be detected even by careful statistical analysis of our final results. What this means in terms of our experiments, is that we must deal with quantities which are beyond the range of experimental error, in order to observe the phenomena. Since you may have somewhat the same problem to deal with, it has seemed wise to me to point this out to you.

I am very much interested in what you propose to do, and I should be even more interested in the results which you are able to obtain. If we can be of any service to you, please do not hesitate to call on us.

Sincerely yours,

Robert A. Kehoe, M. D.

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Reprints under separate cover -

The Plasma-Cell Partition of Blood Lead - Bambach, Kehoe and Logan
Experimental Studies on the Ingestion of Lead Compounds - Kehoe,
Cholak, Hubbard, Bambach, McNary and Story
Editorial Review. Manganese, lead, tin, aluminum, copper and silver
in normal biological material - Kehoe, Cholak and Story
Exposure to Lead - Kehoe