



University of Cincinnati

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DEPARTMENT OF ENVIRONMENTAL HEALTH
Kettering Laboratory, College of Medicine, Eden & Bethesda Aves.

Dr. P. B. Hammond, Professor
Department of Veterinary Physiology
and Pharmacology
University of Minnesota
205 Temporary East of Haecker
St. Paul, Minnesota 55101

Dear Doctor Hammond:

(without evidence)
I am pleased that you are not prepared/to believe my statements concerning the lack of accumulation of lead in the bodies of workmen whose inhalation of lead at a high level is limited to forty hours (more or less) per week. The experiments which were carried out here in simulation of the occupational schedule are, of course, the basis of my conclusion, with respect to the rate of the accumulation. This basis, of course, is not concerned with the difference between ingestion and inhalation, but rather with the intermittent character of occupational exposure to, and absorption of, lead, versus the virtually constant exposure and absorption of lead from the alimentary tract. If the inhalation were of a constant type as it is, with an appreciable variability, of course, in breathing the ambient air (with some concentration of lead therein), the accumulation of lead (appreciable or minute, dependent upon the specific rate of absorption) would be continuous also. In the case of our experiments (and also of workmen), lead is being absorbed at a more rapid rate than it is being excreted for 8 hours per day, while the reverse is true for 16 hours of 5 days per week, and for 2 days at the week end. The result of this is to reduce greatly the weekly absorption of lead, as well as the availability of lead for accumulation. In fact, the rate of this accumulation is too slight to be seen in the living subject, while in the case of animals, it can be seen to have been relatively small, its size depending upon the magnitude of the absorption during the period of high exposure. In fact, it remains so small over a long period of time in the industrial workman, on a fixed schedule, that the concentration of lead in the blood and urine remains at a substantially constant level for many years.

Now, for the evidence of my statements. This lies in the fact that the level of the concentration of lead in the blood (and the actual rate of the urinary excretion of lead also) portrays the status of the labile lead in the body. I fully agree that it does not reveal the concentration of lead in the metabolically inactive

(not actually inactive, but very slight, relatively), lead which is in the dense ivory of the adult skeleton. No means has yet been found for moving this lead from this part of the skeleton. It is believed, and there are a few evidences to strengthen the belief, that the lead here is a part of the lattice structure of this part of the skeleton, and that only the disintegration of the skeleton (Paget's disease, etc.) will release it from this structure. It, thus, is out of the metabolic reactions of the more vascular structure and the more labile bonds of the trabecular bone.

Now, if you will look at the experiments relating to ingestion, you will find that, except for the regular climatic (I suppose) effects, the accumulation of lead is found to occur at an essentially constant rate from year to year, which varies with the

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magnitude of the daily dose of administered lead. And with this accumulation, there is an irregular, but constant, trend toward increase in the rate of the urinary excretion of lead and the concentration of lead in the blood. How can this occur when the rate of administration remains essentially constant for years? Obviously, this can occur only when the difference between intake and output continues to mount accumulatively. This is a crucial piece of evidence, for it means that the head of pressure, so to speak, which induces a steadily increasing urinary excretion, results from the amount of lead accumulated in the body. If no such effect is discernible, then the rate of the accumulation is too slight to be demonstrated by the rate of the urinary excretion or by the concentration in the blood (which mounts at an entirely different rate from that of the urinary excretion, for very good physiological reasons). This is why it is possible to say that the accumulation of lead in our inhalation experiments occurs at an insignificantly low rate (in terms of the bodily metabolism), after the urinary rate of excretion and the concentration of lead in the blood have reached their peak and continue on a somewhat irregular but obvious plateau. It is precisely because the body is not one uniform physiological unit that this is the case. That is, the rate of the accumulation in the dense bone, whereby it escapes from the actively metabolizing part of the body, is the means by which prolonged exposure to small amounts of lead results in the isolation of a small proportional part of what is absorbed, so as, in effect, to remove it from the active physiological medium of the body.

Again, I must say that this physiological situation is responsible for the present means of the protection of workmen from the effects (seemingly from any and all bad effects, in so far as we have the knowledge and skill to observe) when one reduces their exposure to the point at which there is no further increase, after the preliminary equilibration at a safe level (within their working lifetime), in the rate of the excretion of lead in their urine or the concentration of lead in their blood, if the exposure is actually controlled. It can be, and that is the issue. Especially is the latter tissue important, for lead is bound in the erythrocytes according to their chemical and physical characteristics, just as it is in every other tissue in the body, including the skeleton, according to their characteristics. (This appears to be the case, but the relation between the concentration of lead in the blood and those in other tissues has not been decisively demonstrated, as I am fully aware. We are investigating this matter in some detail in dead human bodies. The coroner's office and the morgue are situated in this Laboratory, and, therefore, we have full access - within the limits of the law and current practices - to necropsy material. There is very little information in the literature on this matter.)

I have gone to some length to indicate some of my interpretations of our experimental results. These experiments have never been written up and discussed fully in the literature, for the reason that I have been content to supply the data in illustration of their high points, without full discussion. I should not say "content" for this is not the word; I should say "compelled." I have never had the free time to sit down and write the monograph that is the logical product of our work. I still hope to do it. I think you will agree that the effort to present the observations of many years of intensive work, and the interpretations which derive from them, in so complicated a subject as this, is a formidable undertaking, especially because it is essential to keep up with the experimental and clinical observation of many other investigators and clinicians. I say "our work" because my associates, over the years, have, in many instances, done things which I could not have done, even if I had had the time. This,

B. Hammond

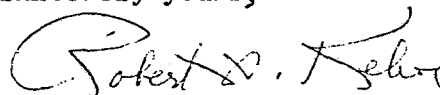
3

October 7, 1971

therefore, is not a modest editorial "we" or "our", but is the true account of the situation. Fortunately, I have been able to visualize and to help in the development of the extension of this work, beyond its present status, and beyond my participation in it, and so I doubt that such an interruption will result in its discontinuance.

Incidentally, the fall-off in the rate of the accumulation of lead by M.R. occurred at the same time of year on each of the succeeding years, in illustration of a seasonal change in the rate of the metabolism of lead. I have commented on this in the Harben Lectures without undertaking to interpret it. It is, however, an important matter, which, at first, came close to misleading me. Fortunately, I waited to find out what would happen later, when as you can see, the earlier behavior resumed, and the alteration later reasserted itself. As you will also see, the decrease in the rate of the accumulation of lead in the body was caused by an increase in the rate of the excretion of lead, whereby the concentration of lead in the blood remained essentially level for a time and then resumed its progressive rate of increase. The irregularities of the curve are a bit confusing and require careful examination.

Sincerely yours,



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

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