CRITERIA FOR HUMAN SAFETY FROM THE CONTAMINATION OF THE AMBIENT ATMOSPHERE WITH LEAD

by Robert A. Kehoe, M.D.

From the Kettering Laboratory in the Department of Environmental Health
College of Medicine, University of Cincinnati, Cincinnati, Ohio

The attention which has been focused, in recent years, on the potential threat posed by the pollution of the ambient air, particularly in urban areas, with numerous chemical and physical products of modern technological developments, has led to a search for satisfactory criteria for defining specific qualities of the air in relation to specific airborne components. One such component is lead, which has been under scrutiny since the middle nineteen-hundred-twenties, but has attracted renewed attention lately.

The immediate question which arises, in connection with the general distribution of airborne lead, has to do not only with the quantity of lead in the respired air, but also with the quantity in the food and beverages consumed by persons in the general population. The crux of the hygienic issue, stated in the briefest possible terms, lies in the possibility that the quantity of lead absorbed into the human body under conditions associated with a larger than usual intake of lead via both the alimentary and respiratory tracts, during any part or all of the span of human life, may lead to the progressive accumulation of a potentially or actually dangerous burden of lead in the body. There is little doubt that present conditions, where they have been investigated, are free of this hazard, but should circumstances combine to provide unusual conditions, now or in the future, whereby relatively large quantities of lead in the air in some areas coincide with relatively large quantities in the food and beverages in the same area, the threshold of safety might be exceeded over sufficient periods of time, with unfortunate results. It has seemed not only prudent, but imperative, in view

of the wide use of metallic lead, its alloys, and its chemical compounds, in modern technology, to develop trustworthy criteria for human safety, with respect to the absorption of lead, as well as feasible methods for the appraisal of the hygienic status of both the environment and the population, in the matter of their content of lead.

Lead in Food and Beverages

The experimental approach to these matters has yielded a reasonably satisfactory appraisal of cross-sectional environmental conditions in the United States of America, with respect to the lead in food and beverages (1), as well as a method for periodic reappraisal, that will yield valid information promptly (1). It has also provided a criterion of safety, in terms of the quantity of lead that can be ingested daily by healthy human adults (under standard conditions with respect to the lead content of the respired air), without incurring the risk of a measureable degree of progressive accumulation of lead in the body (2). The procedure has consisted in a moderate but informative amount of sampling and analysis of common and uncommon articles of food and beverages, plus a demonstration of the representation of these (and other) articles in the regular dietary of healthy young men (of good appetite), through the collection and analysis of composited duplicates of everything consumed day by day over periods of months or years. The general procedure has been that of following the total alimentary intake of lead, as indicated above, and the total output of lead in the feces and urine, in balance experiments that were carried out for periods ranging from 6 months to 4.5 years. Up to this time, 20 healthy individuals have been the subjects of these experiments. The number of the subjects, their variable age and size, and the variety of the dietary habits associated with their upbringing and later experience, has guaranteed a fairly broad portrayal of the composition of the diet of the country, both qualitatively and quantitatively, and of its content of

KE 0013013

lead (1). (In considering the validity of the foregoing statement, one must take into account the nation-wide, year-around facilities for the distribution of food-stuffs in the United States, whereby the principal food markets resemble each other closely in almost all parts of the country.)

Lead in the Ambient Air

A somewhat different type of appraisal of the quantities of lead and their significance, in the ambient air, has been required, and it is with these facets of the general problem that the present discussion is concerned.

It is evident that the application of any criterion of safety, with relation to the absorption of lead from the air, must take account of the absorption from the alimentary tract, and vice versa. It is not very enlightening, therefore, merely to measure the quantities of lead in the atmosphere to which persons in the general population might be exposed, as a means for the appraisal of their exposure to lead. Quite apart from the physical and chemical characteristics of the lead compounds dispersed in the atmosphere, which will exert important influences upon the behavior of the lead in the respiratory tract and upon its ultimate absorption, the quantity absorbed day by day from the alimentary tract, even that increment which may have been derived from the air, must be known. Here, again, as in the case of the lead ingested with food, the only means, or at least the best means, of obtaining precise information, is that of following the respiratory intake and output of airborne lead, on the background of the alimentary intake and output of lead, under well controlled conditions in the laboratory.

An additional troublesome feature of an experimental program involving human subjects, which might be devised in simulation of the exposure to lead in the ambient atmosphere, arises out of the fact that the latter, while variable in time and place, is a continuous process. In view of the virtual necessity of an intermittent type of experimental exposure, in the case of human subjects,

some procedure that would provide a basis for extrapolation from the observed physiological effects of intermittent exposure, to the derived effects of continuous exposure, had to be sought. Because of the regularity, amounting almost to mathematical predictability, of the metabolic responses of human subjects to different known levels of dosage of a specific compound of lead, it seemed likely that a regularly graduated duration of exposure to a known concentration of a known compound of lead, in a known state of subdivision in the air, would yield a correspondingly graduated response from which to determine, by extrapolation, the ultimate response to continuous exposure. This likelihood was tested in an experiment involving detailed observation of two human subjects over the period of 144 and 178 weeks, respectively. (A longer period of preliminary observation of one of the subjects, during the intake and output of lead under standard conditions, enabled the two subjects to undergo their first period of experimental exposure simultaneously, and to continue in parallel observations thereafter.)

Preliminary Experiment

In accordance with procedures developed in previous experiments (3), Subjects J. S. and L. D. were engaged in daily preliminary observations of their metabolic pattern, (intake of lead in food and beverages, and output of lead in the feces and urine), over periods of 56 and 86 weeks, respectively, (these subjects were continued under observation for different periods of time, for the purpose of obtaining more extensive metabolic and environmental data, while the respiratory chambers were being employed in other experiments).

They entered two similarly designed respiratory chambers, into which air containing 150 micrograms of lead per cubic meter, as the sesquioxide, in particles ranging up to 0.18 micron in diameter, and having the mean diameter of 0.05 micron, was being introduced and distributed in a uniform manner. The design of the experiment called for exposure to these conditions on the following schedule: 16 weeks for 10.5 hours per week; 16 weeks for 21 hours per week; and so on, 16 weeks at a time,

KE 0013015

for 31.5, and 42 hours per week.

During each successive period of 16 weeks, as had been the case in every other experiment involving intermittent exposure in simulation of occupational experience (i.e., 40 hours per week) (3), the level of the output and concentration of lead in the urine, as well as the concentration of lead in the blood, rose up to a certain point and then continued at an essentially constant level, so long as the conditions of exposure remained constant; each incremental increase in the weekly duration of the exposure resulted in a further increase of the same proportions in the output and concentration of lead in the urine and in the concentration in the blood; a line connecting the points representing the final levels of the concentration of lead in the blood achieved in successive periods of 16 weeks, continued as a straight line of uniform slope. The results of the extension of this line, at the same slope, to a point that corresponded, in each instance, to continuous exposure (168 hours per week) is shown in Figure 1, (Subject L. D.), and in Figure 2,(Subject J. S.). The analytical data of this experiment have been assembled and charted in Figures 3 and 4,(Subject L. D.), and in Figures 5 and 6,(Subject J. S.), for such information as they can provide, without discussion herein.

On the reasonable assumption that the type of extrapolation employed here portrays, with approximate faithfulness, the probable outcome of actual exposure to the projected conditions, several highly important facts emerge from these observations. First, the similarity in the behavior of the two subjects under substantially identical experimental conditions is striking. Second, the steady increase in the physiological response of the subjects to an increase in the one variable, time, is very revealing in both physiological and practical terms. Third, as we have noted previously (3), the fact that intermittent exposure at a certain level can and does result in an equilibrated response, is a most important factor of safety in occupational exposure to lead, but this factor is not operative

KE 0013016

in the general environmental situation. And finally, the gross difference between continuous and intermittent exposure to lead, with respect to the absorption of lead, is a matter to ponder seriously, in relation to the lead content of the ambient atmosphere. It is evident that the only certain provision for human safety, with respect to continuous exposure to lead, lies in the avoidance of a persistent level of alimentary and respiratory dosage that will result in a measureable accumulation of lead in the bodies of exposed persons in the course of a life time.

The results of this experiment achieve their greatest practical importance, however, in indicating the feasibility of this method of investigation, for determining, approximately, the maximum concentration of lead in the ambient atmosphere, (in association with the current intake of lead in food and beverages), that is compatible with human health and well-being. The promptness and the quantitative orderliness of the physiological response to graduated severity of exposure, as represented by the increase in the rate of the excretion of lead in the urine or, more strikingly and more certainly, by the increase in the concentration of lead in the blood, demonstrate, clearly, the reliability of this criterion as a measure of the absorption of lead. It is likely that the linear extrapolation, from the observed responses induced in the subjects by intermittent respiratory exposure, to the projected end point in continuous respiratory exposure, errs somewhat on the low side. The establishment of an equilibrium between the intake and the output of lead, in association with intermittent exposure, results, doubtless, from the balance achieved, at some point in time, between the periods of exposure, when intake is greater than output and lead is retained in the body, and the periods of freedom from exposure, when output is greater than intake and lead is lost from the body. As the period of exposure lengthens progressively, and the period of freedom from exposure shortens progressively, (as in this experiment) the loss of lead from the body, during the period of freedom from exposure, will tend to fail more and more to balance the absorption, and the graph indicative of the

KE 0013017

increasing concentration of lead in the blood may be expected to deviate from a straight line and assume an upward concavity. For this reason, this end point has been designated above as an approximation.

Critical Experiment

With the evidence of the foregoing experiment at hand, a further experiment was designed in an effort to determine the level of continuous exposure to airborne lead, under previous experimental conditions, with reference to the compound of lead, (the sesquioxide), in a nearly ideal state of subdivision in the air, (mean diameter of 0.05 micron), for its retention and absorption in the lung, that would barely yield a response, in the form of the least statistically valid increase in the urinary excretion of lead, without a corresponding increase in the concentration of lead in the blood. (It has been shown, previously, that the earliest evidence of an increase in the absorption of lead by the intact human organism is a measureable increase in the rate of the excretion of lead in the urine (3).)

Two new subjects were investigated, as to the pattern of their intake and output of lead under standard conditions in the laboratory, one, (Subject N. K.), over the period of 29 weeks, and the other, (Subject S. S., at a somewhat later time of the year), over the period of 19 weeks. Following these preliminary observations, which demonstrated the suitability of the subjects, they embarked upon a parallel schedule of respiratory exposure to lead, (parallel in type but not in time), in the concentration of 10 micrograms of lead per cubic meter of air. The temporal schedule, as a rule, involved 16 weeks of exposure, at each of a prescribed series of weekly rates, (10.5, 21.0, 31.5, 42.0, 52.5, 63.0, and 73.5 hours, per week), although, in two instances, for different reasons (the convenience of a subject, a short vacation, or the desirability of extending a period of exposure so as to check on its adequacy in disclosing the peak of the physiological response), the schedule of each subject was interrupted or altered

KE 0013018

slightly.

The terminal results of this experiment are not available as yet, but the sequence of the more significant events during the total period of the exposure of (Subject N. K.), and during all but the final period of the exposure of the other (Subject S. S.), are portrayed in Figures 7 and 8 and 9 and 10, respectively. There appeared to be a slight increase in the output of lead in the urine and in the concentration of lead in the blood of both subjects, as the experiment progressed. The increase was irregular, late in putting in its appearance in the case of Subject S. S., and of such slight proportions in both instances, as to be of dubious significance. The data reveal trends, however, which would seem to be sufficiently persistent to be valid. Unfortunately, their interpretation is uncertain, for the reason that the lead content of the food and feces of both subjects was variable, and the increases above the average level tended to coincide with the increases in the output of lead in the urine and the concentration of lead in the blood. In neither case was it possible to plot a curve that would fit, adequately, the findings in either urine or blood, from which a seemingly valid extrapolation could be projected. It may be that the concentration of 10 micrograms of lead in the air is near the threshold value which is being sought in these experiments. Another experiment, at a level of atmospheric concentration sufficient to yield definitive results (at least four points on a curve from which to extrapolate), will be required to elucidate this matter.

The purpose of this presentation has been to describe a method for the investigation of a troublesome and significant issue in environmental hygiene, rather than to give results in such detail as would be required to be decisive. A more elaborate examination of results, both those now available and those yet to be obtained, must be forthcoming later. It is gratifying, however, to envision, however incompletely, the near achievement of a long sought goal.

KE 0013019

References

1. Kehoe, Robert A.: The Harben Lectures, 1960. Lecture I. The Normal Metabolism of Lead. J. Roy. Inst. Public Health, 24:81, 1961.

2. Kehoe, Robert A.: The Harben Lectures. Lecture III. Present Hygienic Problems Relating to the Absorption of Lead. J. Roy. Inst. Public Health, 24:177, 1961.

3. Kehoe, Robert A.: The Harben Lectures. Lecture II. The Metabolism of Lead under Abnormal Conditions. J. Roy. Inst. Public Health, 24:101, 129, 1961.

KE 0013020