

The Physiological Tolerance of Apparently Healthy Human Individuals for the Daily Absorption of Inorganic Lead Salts Over Extended Periods of Time

Introduction

It has been known for centuries that the absorption of inorganic compounds of lead, in sufficient quantities, under appropriate circumstances, and over considerable periods of time, are capable of inducing poisonous effects upon man. It has also been recognized that lead poisoning, generally, while not, necessarily or generally, a violent intoxication, has induced serious consequences in many instances, especially among children. Moreover, while the responses of individuals to the absorption of lead have appeared to be highly variable, they have developed slowly, in the main, notably under the conditions of occupational exposure. Indeed, these characteristics of this intoxication, in themselves, have been responsible, in considerable measure, for the highly unsatisfactory handling of the hygienic problems of lead in industry and in the community at large, in both of which, for such a long time, they have affected mankind.

Initiation of This Experimental Program.

In 1937, a group in the staff of the Kettering Laboratory, (an offshoot of the Department of Physiology, in the College of Medicine of the University of Cincinnati), under the guidance of Assistant Professor ^(Physiology) Robert A. Kehoe, M.D., who as Director (and founder) of the Laboratory began a broad investigation of the behavior of human subjects under the ordinary conditions of their day-to-day intake of lead (so far as this could be achieved) and the output of lead in their feces and urine, ^{with the following limitations:} In earlier and later years, a substantial effort was made by staff members in the Laboratory, to deal with industrial situations involving the use of lead, (and also with many other chemical (hygienic) problems of industry).

The ^{incident} exposure of infants and preschool children to lead was also investigated in association with physicians of the Children's Hospital (Cincinnati) and other community medical services, and the clinical aspects of lead poisoning, in this connection and generally, were studied in detail.

In the course of these investigations, physiological, clinical and analytical observations were made on a very considerable number of apparently normal individuals, young and old, male and female, and it began, first dubiously, and later, more evidently, to appear that all persons, in utero, at birth and later, in the North American population, had absorbed lead in some quantity, as evidenced by lead in their feces and urine, in their blood, and in their tissues, with a fairly characteristic distribution (dependent upon various factors, not always readily established in either the living or the deceased). With the further development of information and chemical and clinical methodology and with further facts obtained by other competent investigators, it appeared likely that all men and all living things, sustained on a planet composed in part of lead compounds, might well have lead in their composition. It seemed worthwhile, however, to investigate, if possible, a segment of human society characterized by a more primitive life than that of modern United States of America.

In 1932, such a society appeared to be available in Mexico, D.F. In the rural area of Ixtahuaca, one and then another Indian community, living under remarkably primitive conditions, were found and investigated. The results of this investigation have been reported. These facts, along with scattered observations made by ourselves and other investigators would seem to justify, fully, conclusions that lead, in the soil of the earth and in ^{it} the waters, in its vegetation and animal life thereon, including that of man, and in its atmosphere, is and has, for a long time, been a regular and essentially normal constituent. That this constituent has sustained some increased degree of availability to earth's flora and fauna in modern times, seems apparent, but the degree of any such increase is minute and its actual hygienic significance, at this time, or in the foreseeable future, is much more a matter of unsupportable opinion than of

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evidence. This fact, one hastens to say, is not reason for the relaxation of the continued acquisition of information on the current status of the matter.

The primary purpose of this investigation of human subjects was to observe, quantitatively, over prolonged periods of time, the metabolism of lead administered to normal, healthy adult human beings, under controlled conditions, with as little interference with their ordinary behavior as might be possible in compatability with their safety and comfort.

In view of the inevitable variability in the behavior of individuals, it was necessary to visualize the degree of such variability by observing numbers of individuals, not necessarily large, but, hopefully, sufficient numbers, with respect to age, (avoiding unduly old - i.e. retired and especially somewhat decrepit or ill persons and selecting apparently normally functioning individuals); males, predominantly, were selected for reasons of convenience; but one female, a negress, was employed; several male negroes were available. The objective, here, was the establishment of facts on which standards and specification for the safety and health of exposed people could be based. In the consideration of such standards and specification, the complicating factors of human variation, and, especially, certain voids in the available physiological information, gave rise to dissatisfaction with the methods employed and the results obtained in fact-finding surveys conducted by ourselves and others. The conclusion was arrived at, reluctantly, that it was necessary to approach these matters in a direct manner so as to arrive beyond the present unsatisfactory situation into future predictable prospects. It seemed both wise and essential to set up experiments of broad scope wherein under carefully controlled conditions, human subjects should be subjected, in sufficient numbers and types, (with the exception of infants and children of tender physical age) to cover, hopefully, the variability of

human responses to the ingestion and inhalation of suitable chemical compounds of lead, day, after day over considerable periods of time. If there should be reluctance, on moral grounds, to engage in such experimentation, one need only contemplate the current and increasing frequency of the introduction of thousands of persons into employment in the lead (and other) trades in which, with few exceptions, relatively speaking, the physical and chemical (physiological) hazards have been largely unexplored and (of course) inadequately controlled. It was, indeed, quite clear that standards worthy of acceptance and capable of application, cannot otherwise be applied generally, not even to mention the medical and hygienic mechanisms for the achievement and maintenance of such standards. A conscientious physician investigator could not expect to subject other than willing and informed human subjects to such an experimental regimen as might be employed, despite the knowledge of the experimenter, based on experience, which would ensure of any experimental procedure which involved significant risk of an unpredictable outcome.

In view of the primary investigators' obvious inability to know all or much of the previous life experience of the subjects, it seemed wise to select, so far as possible, persons whose apparent life histories appeared to indicate their freedom from unusual or obviously severe (primarily occupational) exposure to lead at any time in their lives, and especially in recent (4 or 5) years. Thus, persons with whom this investigator was well and agreeable acquainted, especially members of the service and technical staffs of the Kettering Laboratory, were desirable subjects, both because of his familiarity with an appreciable portion of their lives, and because of relationships which provided information as to their personal reliability in response to instructions, as well as their general trustworthiness, and our mutual respect. Thirteen of the sixteen subjects fitted into this category, and it was not difficult to find three others of corresponding character. Three others, for one reason or another, did not complete their assignments in this role. None of the sixteen manifested any anxiety at any time in the course of

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these experiments, nor any reluctance to follow their instructions as experimental subjects.

Specific Problems Under Consideration In This Experimental Approach

1. The poisoning of infants (unborn and after being born), and of children of preschool age, with lead is, clearly, in its present stage, not one of discovery or of diagnoses, but one of prevention. It is evident, even assuming, as one may well do, that lead in minute quantities, is a normal constituent of the tissues of all members of the human species, that women, unmarried or married, of child-bearing years, must be shielded from any undue or abnormal exposure to lead compounds. There is no doubt that this preventive procedure will be difficult to apply, in present-day society, but there is little doubt that it can be achieved, very largely, almost at once, if there is a social will to do so, and that the effect may be more complete, with but rare exceptions, within a short period of years.
2. The hazard due to the presence of lead in the general environment, in the air, particularly, if existent at all, is quite small. The setting of suitable standards, at present, for the safety of the population ^{of the United States of America,} is feasible, and an adequate program of monitoring seems not prohibitively difficult, ^{for} or excessively expensive. A complex industrial society such as ^{that of the United States} our own, can hardly exist in safety, without certain programs of this type in relation to certain widely occurring materials.
3. It is obvious that occupational health, in any modern nation, has become a stern necessity for its survival. As the lives of the people and their activities, especially their industrial activities, become more and more complex, the means of ^{the people's achievement of} their achieving healthy lives becomes more and more exacting. Such situations demand the development of hygiene and medical

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^{efforts} efforts in sufficient numbers and types for their control (or be spot)
 of the existing hazards, as a matter of public policy. The actual hazards
 to the health and welfare and the very lives of the employees of the
 industrial organization in the United States, (and in the other nations of the
 earth) are too numerous and too variable even to classify^{ed} at the present time.
 They are increasing in number and severity^{in the} and a virtually heroic^{effort} effort
 will have to be forth coming^{soon} to bring them under a reasonable degree of
 control. In this nation because of its historic development from too loose^{individual} and too atomistic
 an association of States, which, for many reasons, retained much of their inde-
 pendence, while being forced by circumstances to develop nominal^{legal} unification.
 Only recently (19) has the responsibility for Occupation Health become
 a federal function, while during these too lengthy intervals of State authority,
 the functional usefulness of industrial State efforts have ranged from near
 zero to good (on their surfaces), without, in any case, ~~from adequate~~^{adequate}
 health services^{for} to industrial employees. Certain individual industrial
 organizations^{through} and their responsible personnel, on the other hand, have
 succeeded in pointing the way toward a future goal, while a few professional
 pioneers, who can almost be numbered on the fingers of one's two hands have
 provided the impulse to project Industrial Hygiene and Industrial Medicine
 as respectable fields of professional specialization. It is imperative, at the
 time that the toxicological potentials of the large numbers of new and old
 chemicals products and the many physically injurious products and techniques
 of industry be investigated by competent persons and groups, so as to catch-
 up as nearly as possible and as soon as possible. It is equally urgent that the
 essential characteristics and the variability of the human responses to the
 bodily absorption^{of} impact of these chemicals and physical agents be
 established on sound physiological and clinical bases. By such means, in time,
 (and the time must not be too long in view of the urgency), the dual but
 first approach of the Industrial Hygienist and the Industrial Physician can be

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established within the actual industrial scene.

Certain Aspects of Present Information Concerning the Absorption of Lead into the Human Body, its Distribution Therein and its Elimination Therefrom,

The significance of lead, in the world of mankind at the present time (1977), is determined as much in specific parts of the world, and in specific areas of its nations as by the physiologic characteristics of the human organism. It is necessary, therefore, to assess the influence of various features of the exposure of man to lead in order to understand its behavior.

There are, in likelihood several natural types of the exposure of man to lead in modern developed societies, namely, the current incidental exposure occasioned by the natural characteristics of the earth and its atmospheric envelope, and the changes which have occurred and will continue to occur herein through natural or elemental alterations such as, for example, earthquakes, storms, floods, etc. Since such effects have not been assessed in the past and are unlikely to be separated out in any strictly quantitative or proportional manner in the future, so far as the present writer can discern, such alterations are necessarily to be combined with any modern variations of the presence of lead in the environment of man.

Under environmental exposure to lead, therefore, we shall include, for present purposes, that exposure to lead which is purely incidental, so far as his ordinary experience of living and breathing, under ordinary circumstances, consuming food and beverages, including water, for his subsistence, clothing and housing himself normally, and persisting

The Absorption of Lead by Man

All absorption of lead by man is of environmental origin, in the sense that it is derived from the human surroundings; but there is not, actually only one environment. Thus, the infant, in utero, is subjected to the absorption of lead, only via the placenta, from the maternal blood stream, while, after birth, the sources of such exposure are on the earth and its atmosphere. Even under the conditions of independent life, however, the sources of exposure differ grossly, in their proportional representation in the manner or degree of their impact upon different groups in the population at large. The ingestion of lead from its presence, in crumbling paint, for example, on the external surfaces of objects in the environment of the exploring infant, or the child of pre school age, whose surroundings are often not too ideal and whose supervision is often somewhat neglected or at least none too wise or careful; the disproportion between the respiratory and alimentary exposure to and absorption of lead by the occupationally employed; and the opposite pattern of the quantitative relationship between the absorption of lead from food and that from the atmosphere (usually both combined are harmless); there thru situations furnish examples of the variations in type and significance, quantitatively. Infantile exposure to lead, almost unique in type, is often highly dangerous both to life and to the future ability of survivors. Occupational exposure need not and should not be dangerous, although at present, often is., while the exposure to lead by the ^{general} ~~general~~ adult population of the country, commonly referred to as Environmental Exposure to lead, may only be conceived of as potentially dangerous i.e. in future time.

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Environmental Exposure to Lead

It should be recognized that the Environmental Exposure to lead in the United States of America, at present, (and actually for along time in the past) includes some indeterminable quantity beyond natural and primitive sources, ~~and~~ consisting of the contributions which have resulted from contamination of the earth- its stones, soil, water, and atmosphere, with lead derived from various activities of man, in his choices, ^{choices, such as the} ~~and~~ use of land, forest, streams, lakes, seas, mines and air, in whatever manner, thus far, these have been ^{found to be} ~~feasible~~ useful, and desirable. Food and food products and water in its primary and ultimate usages, have contained minute quantities of lead, to which, in a great variety of ways, ^{minute} ~~minute~~, and sometimes ^{relatively} ~~large~~, quantities of lead have been added. At almost every step in the production, processing, ^{ag.} ~~packing~~ and preparation of food for consumption, ^{the} ~~the~~ opportunity ^{is} ~~is~~ for the contamination of ~~food~~ exists, and it would not be remarkable that it had occurred. Actually, however, the low solubility of most of the natural ~~and~~ and otherwise available salts and ~~the~~ ^{lead} ~~oxide~~ of ~~these elements~~ have reacted more significantly than has human effort, in limiting the distribution and ^{human} ~~human~~ absorption of lead from the ⁱⁿ ~~source~~. Thus it has been only since this metal came into production and commercial use that it has demonstrated its proclivities for harm. From the productive processes (chemical and ^{mechanical} ~~metal~~) ~~compounds~~ required to display its unique usefulness came, (somewhat slowly and incompletely), the revelation of its toxicity. Unfortunately, the full scope of the latter properties of lead have been shrouded in some degree of obscurity ^{because of the variety of the human response thereto} ~~for both technological and biological~~ reasons.

The significant environmental exposure to lead of all but the infantile segment ~~(as referred to here)~~ of the population of the United States of America, occurs by way of the alimentary and respiratory tracts i.e., by

way of the ingestion of lead with food and beverages (and with any other ingested materials), and by breathing air contaminated with lead / in vapor form (uncommonly) or in particulate form (regularly and variably). (This is not to imply that lead is not ^{taken in} ~~respired~~ and absorbed in the respiratory tract, nor that the percutaneous absorption of lead does not occur at any time in either infants or adults. Rather, these do not occur with sufficient frequency or magnitude to be of practical hygienic significance, or to be dealt with experimentally in the manner employed in these observations).

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