An Appraisal of the Lead Hazards Associated with the Distribution and Use of Gasoline Containing Tetraethyl Lead.
Part I

By

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Introduction and Acknowledgments.

The development of a motor fuel containing tetraethyl lead raised certain questions in industrial and public health which have claimed an unusual amount of attention. Since 1924 members of the staff of this laboratory have carried on a series of studies of the hazards associated with the manufacture, distribution, and use of this type of gasoline. From time to time (1925, 1927, and 1928) reports of these studies have been made to the Ethyl Gasoline Corporation and the United States Public Health Service, but the accumulated information has not been published partly because of the unwieldly volume of data, and partly because the results of successive investigations were essentially similar to those described by other workers. Thus our conclusions have not differed materially from those reached through animal experimentation by Sayers and his associates (1), or from those arrived at by Leake and other workers of the United States Public Health Service (2) through the use of methods generally similar to ours. Our data (to 1928) and those of Sayers and Leake were critically reviewed by the Ministry of Health of Great Britain as indicated in the Final Report of the Departmental Committee on Ethyl Petrol (3), issued in 1930.

Recently, it has become evident that more definite conclusions are justified with regard to the lead exposure derived from the use of leaded gasoline. Accordingly, in the following pages we observations, made in 1929, which continue our earlier investigations. In a second article we shall present the results of a later and more precise method of measuring the lead exposure specifically due to lead in gasoline in the various occupations which are concerned.

We wish here to acknowledge an indebtedness to our associates for assistance in various items of the work; to W. F. Machle, L. W. Sanders, L. J. Schradin and W. E. Brown for their help in making the physical examinations; to L. W. Sanders for the study of blood films; and to T. J. LeBlanc for the statistical analysis of the data. The expense of this work was borne by the Ethyl Gasoline Corporation in accordance with an agreement between the Board of Directors of the University and officials of the Ethyl Gasoline Corporation.

The Nature of the Lead Hazards.

At an early stage in the use of gasoline containing tetraethyl lead it became apparent that the manufacture of tetraethyl lead and the blending of the concentrated fluid for use in gasoline was a hazardous occupation with unique opportunities for the rapid development of lead intoxication. The serious dangers of these manufacturing processes have no relation to the problem with which we are concerned in the present discussion. However, the initial confusion of the actual hazards of manufacture with the problematical dangers arising from the use of the finished fuel, has persisted. Therefore the distinction between them must be made clear.

Hazards Associated with the Manufacture of Tetraethyl Lead and Leaded Gasoline.

Pure tetraethyl lead is a heavy, colorless, oily liquid which is retained with difficulty within jointed receptables and pipe lines. It is insoluble in hot or cold water, but readily soluble in alcohol and acetone and miscible in all proportions with fats and oils. As might be suspected from the latter, it penetrates the unbroken skin.

Indeed skin absorption alone may result in the rapid production of acute illness and death in experimental animals (4,5). From a physical point of view, the volatility of tetraethyl lead is low, but in toxicological terms it is dangerously high, since at ordinary temperatures air saturated with its vapor contains approximately 5 mg. of lead per liter. This concentration is lethal for rabbits in a few hours (4), a fact which demonstrates the ease with which tetraethyl lead penetrates the pulmonary epithelium. Under certain conditions, notably in the presence of sunlight, tetraethyl lead is unstable, breaking down to yield water-soluble, crystalline triethyl lead compounds. Slight agitation serves to suspend these fine crystals in the air, when in a dry state, thereby producing a dust hazard which has the quality - unique among lead hazards - of providing warning of its presence, in that a very low concentration of these substances induces irritation of the mucous membranes with weeping and sneezing.

The dangers associated with the preparation and handling of tetraethyl lead are fairly obvious, when these properties are recognized. Unfortunately, this information was not available when the manufacture of the product was first contemplated. It is not strange, therefore, that when the production of tetaethyl lead emerged from a laboratory scale into an incipient commercial stage, cases of lead poisioning odcurred, characterized by the sudden onset of cerebral symptoms and a high mortality.

Without entering into a description of the various steps by which leaded gasoline is prepared for the market, suffice it to say that the hazards of manufacture are due mainly to tetraethyl lead. The hygienic problem at every point consists in the prevention of skin contact with tetraethyl lead, and in the maintenance of conditions under which its vapor is not inhaled. Because of the sharp localization of the dangers, they are amenable to adequate control; nevertheonly by continual vigilance. The extent to which lead absorption has been controlled in the manufacture of tetraethyl lead through the use of special equipment and through the inauguration and operation of suitable safety measures has been shown elsewhere (6).

Hazards Associated with the Distribution and Use of Gasoline Containing Tetraethyl Lead.

The hazards associated with the handling and use of the finished gasoline differ both in quality and quantity from those which occur in its preparation. Nothing could demonstrate the difference in the magnitude of the potential lead exposure of the two sets of conditions in a more pragmatic manner than the failure on the part of such gasoline to produce a substantiated case of lead intoxication up to the present (November, 1933) after more than 10 years of continuous use in certain parts of the United States and almost 8 years throughout the entire United States. (This basis of differentiation is the more significant when one considers that the hypothetical opportunities for the absorption of lead, as a result of the distribution of leaded gasoline, are so varied and so widespread as to defy regulation.) But there are other points of difference which did not require the test of experience for their recognition. Tetraethyl lead is introduced into gasoline in amounts so small that the solution lacks the essential toxicalogical properties of tetraethyl lead. Thus, whereas tetraethyl lead alone, or in high concentration in gasoline, is rapidly absorbed through the skin, its absorption is retarded greatly by dilution in gasoline . Indeed we have been unable to obtain evidence of lead absorption through the skin of experimental animals after their prolonged exposure to concentrations of 1 part of tetraethyl lead per 1000 parts of gasoline by volume (5). The dilution of tetraethyl lead with gasoline also largely eliminates the danger of lead inhalation.

The difference between the volatility of tetraethyl lead and the various gasoline bases with which it is mixed, is so great that approximately half the gasoline may be evaporated before lead can be found in the vapor *. It follows, from this fact, that the vapors rising from tanks containing leaded gasoline do not contain appreciable amounts of lead. However, this does not mean that no tetraethyl lead may be evaporated under any of the practical conditions of handling and use or spillage of lead-containing gasoline.

Although years of experience have not shown the existence of danger to the community in the use of gasoline containing tetraethyl lead, and although the qualities of the fuel, as described above, explain this result in a large measure the possible lead exposure associated with the general dissemination of such a product may not be dismissed lightly. A full appreciation of the opportunities for exposure is required for an understanding of the problem which they provide for investigation.

Leaded gasoline is handled at refineries, bulk storage plants, filling stations, and in public and private garages. It is transported from one to another of these sites in tank ships, tank cars, tank trucks, barrels, and tins. In the United States and in Canada an overwhelming proportion of this motor fuel is dispensed through filling station pumps. In England a large amount of gasoline is distributed in two-gallon cans which are filled by automatic equipment at refineries and at storage points. Large numbers of persons come in contact with the gasoline through spillage, as an unavoidable result of the various methods of distribution. They also inhale vapors from tanks, hose lines and

*We have found that no accumulation of lead occurs in rabbits as the result of months of exposure for several hours daily to such vapors, in experiments in which the gasoline vapors were sufficiently concentrated to maintain the animals in a state of mild intoxication.

surfaces on which the gasoline is spilled. At refinery loading racks, at filling stations and at other points where gasoline is handled regularly, the repeated spillage of gasoline containing lead may bring about the accumulation of higher boiling petroleum fractions, and small amounts of tetraethyl lead, by reason of their absorption into wooden platforms or other surface materials such as concrete, asphalt, gravel, cinders or earth. Under these conditions some portion of the tetraethyl lead is evaporated slowly, and the remainder undergoes decomposition. In either case, opportunity for inhalation of lead on the part of persons in the vicinity may be provided, though, no doubt, most of the accumulations are dissipated by frequent hosing, or by rainfall.

Under prevailing marketing conditions, the decomposition of the tetraethyl lead in gasoline is almost inappreciable, but over a period of years, variable amounts of lead deposits may be found in the scale on the sides and at the bottom of storage tanks, tank cars, and other containers. Attempts to clean these containers in a dry state may cause the inhalation of finely divided dust containing triethyl lead salts. In general, the precautions which are required to prevent the inhalation of dangerous amounts of gasoline are adequate safeguards against the absorption of the lead deposits, but this potential source of lead absorption may not be ignored.

The sale of the gasoline to the consumer takes it into the province of the general public where some degree of exposure to skin contact and to vapors may occur. Of more importance, however, is the appearance of a new set of conditions based upon the combustion of the fuel. Tetraethyl lead is converted, thereby, into finely divided inorganic lead compounds (chiefly lead bromide), which are deposited, in part, along the exhaust system, but which otherwise, are discharged into the atmosphere with the exhaust gases of the motor. The extent of the accumulation of exhaust gases from many automobiles in busy city streets, and especially in poorly ventilated areas where cars operate in considerable numbers, becomes a question of importance. This aspect of the matter concerns the entire urban population, but it develops a special significance in the case of garage mechanics. Garages, in general, are poorly ventilated. Few of them, indeed, are equipped to maintain an adequate dilution of exhaust gases under the most favorable conditions, and when doors and windows are closed in cold weather, ventilation is often negligible. For this reason, through the winter months, many mechanics develop late afternoon headaches from the absorption of carbon monoxide. Their exposure to lead in the exhaust gas of automobiles burning leaded gasoline is greater, therefore, than that of any other group of persons in the community. Further, the handling and the spillage of gasoline, the adjustment of carburetors, and the repair of other parts of the car often involve skin contact with the gasoline and with lubricating oil which may contain minute amounts of tetraethyl lead. The spillage and evaporation of gasoline may leave behind the less volatile tetraethyl lead to be slowly volatilized at a later time, or to decompose, and by so doing to add to the lead dust in the garage. In the dismantling of motors the combustion products of tetraethyl lead may be encountered by the mechanic, and although these cannot be absorbed through the skin, they may be a means of contaminating his hands, his clothing, and his surroundings. We must regard these factors, as well as the deposited lead of the exhaust gases, as contributors to the accumulations of lead dust within the garage although the amounts of lead involved are probably not so great as those which originate from the repair of electrical storage batteries and the use of paints and solder in the repair of automobiles.

One further point must be considered in a complete analysis of the possibilities for general lead exposure in the use of gasoline containing lead. The deposition of lead compounds upon the highways, city streets, - in short, upon the surface of the earth - may conceivably influence the amount of lead breathed by animals and men, as well as the quantity incorporated in and deposited upon vegetation employed as food.

The Distribution and Sale of Leaded Gasoline in the United States.

The character of the lead hazards developed through the use of leaded gasoline is based upon the methods of its distribution and use. Their general magnitude is dependent upon the extent of the distribution of such gasoline, the volume of consumption in a given area, and the period of time over which distribution and use have extended, these factors being modified to some extent by the variations in the lead concentration in gasoline, which have occurred in various sections of the country.

Gasoline containing tetraethyl lead was distributed first in the early months of 1923 in Dayton, Ohio. A few months later it was on sale in Cincinnati and in the district about these two cities. Thence its use was extended to middle western and southern United States, into areas represented most satisfactorily by the cities of Chicago, Detroit, St. Louis, Jacksonville, Atlanta, and Savannah. The quantity of this gasoline sold up to 1926 cannot be estimated accurately, but it was limited to this general area, and there was a steady increase in the volume of distribution during this time except for a period of almost a year beginning in May, 1925. (At that time leaded gasoline was withdrawn from the market pending an investigation of the United States Public Health Service, though for various reasons its use was not interrupted in certain areas.) The expansion continued until this automobile fuel had become available in all parts of the United States. Table 1 shows the dates at which sale began in various cities of the United States. The duration of continuous distribution for these areas is also recorded up to the time of the observations which are to be described. The approximate quantities sold during the years for which figures are available are shown in Table 2. It should be noted that the general areas into which the gasoline was first introduced maintained the largest proportional and gross consumption.

In Ohio, where the greater part of the early investigations were carried out, the concentration of tetraethyl lead in gasoline up to 1926 was maintained at 3cc. per gallon - approximately 1 part of tetraethyl lead in 1260 parts of gasoline, by volume. In certain other areas, during this period, as little as 2 cc. was used. Since that time, the lead concentration has varied in accordance with the quantity required to bring the available gasoline base up to a definite standard of performance in a test engine, except that the amount introduced has not exceeded 3 cc. of tetraethyl lead per gallon of gasoline. The average lead concentration by years for different regions of the country may be seen in Table 3.

A brief study of the contents of these tables is sufficient to give a clear indication of the areas in which the greatest opportunities for lead exposure have been provided. They also yield a graphic concept of the proportions of the problem with which we are dealing.

In the light of the information furnished by previous investigation, there can be little doubt that certain of the hypothetical hazards described above, do not exist. However, we shall disregard these details and deal, primarily, with one question, namely, - is the magnitude of lead exposure arising from the combined hazards of the use of leaded gasoline such as to bring about appreciable lead absorption on the part of any group of individuals in the community?

3. Experimental Investigation.

The Selection of Experimental Subjects.

Groups of subjects were selected for detailed study of the effects of their occupation upon their health, and upon such physiological processes as are specifically influenced by an increase in lead absorption.

Table 4 shows the numbers and types of subjects, together with the locality in which they were employed. The three groups of workmen who had experienced all the types of lead exposure associated with the use of leaded gasoline are represented by 56 filling station attendants, 50 tank-truck handlers of such gasoline, and 201 garage mechanics.

The filling station attendants were chosen with attention to several matters: men who had been employed as subjects previously, who had been handling leaded gasoline for the longest period of time, who had handled gasoline containing the highest concentrations of tetraethyl lead, and who had handled the largest amounts of leaded gasoline daily, were especially desirable. Until May 1925 a small metering device containing a liter can of Ethyl Fluid was used on filling station hose lines to treat gasoline with the lead mixture as required. This method of distribution brought about some degree of exposure to concentrated tetraethyl lead on the part of filling station employees. Therefore, those subjects whose employment dates back to this period have had opportunities for the absorption of lead from this source. They were particularly favorable subjects for the determination of the maximal lead exposure associated with their occupation. It has been pointed out previously that in the cities of Dayton, Cincinnati, Savannah, Jacksonville and Atlanta there had been no interruption in the distribution of leaded gasoline since its introduction. Futhermore the employment turnover of filling station attendants had been such that it was not difficult to find a satisfactory group of men who had dispensed leaded gasoline since it was first marketed from their stations. The consumption of leaded gasoline has been greatest in certain central states represented by the cities of Dayton, Cincinnati, Detroit, Chicago and St. Louis. In these cities individual attendants at certain well located filling stations had handled more leaded gasoline than had men similarly employed in any other part of the country.

The tank wagon handlers were selected on the basis of the severity and length of their exposure to leaded gasoline. Twenty-four of them had served as subjects for study in 1927. Thus a direct comparison of the results obtained on the two occasions was made possible.

The garage mechanic group was made up of 109 persons who had been working on cars which used only leaded gasoline, and an additional 93 who had been repairing cars of which a high percentage used such gasoline. Effort was made to find all the mechanics in the United States who had experienced prolonged exposure in garages in which all the cars had used leaded gasoline exclusively over a period of several years. Ten members of the group had been employed in a public service garage in Dayton, Ohio, in which only leaded gasoline had been used from 1923 to the time of the present investigation. Thirty-nine subjects had had from 3 to 6 years of daily repair work on cars in which leaded gasoline was the exclusive fuel. The entire group was composed of subjects who had been employed in continual repair work on fleets of cars.

From every point of view the subjects selected for examination had the maximal opportunity for exposure to lead arising from their respective occupational relationships to leaded gasoline. The garage [illegible] is entitled to special consideration since it is composed of men whose occupation combines all the potential lead exposure derived from the gasoline in an intensified form, together with certain other lead exposures which are not related to gasoline. For this reason it was expanded to a large number at the expense of less exposed groups.

The barrel-fillers referred to in Table 4 are included among the subjects for a specific reason which will appear later. The data are available through a fortunate combination of circumstances. Several years of observation of persons whose occupation involved considerable exposure to gasoline had aroused our interest in the influence of prolonged gasoline absorption. Accordingly, a search was made for a group of subjects whose exposure to gasoline was severe and uncomplicated by other occupational factors. In the summer of 1928 such a group was found in a refinery in which large quantities of gasoline were put into fifty gallon barrels for transportation. The barrels were filled in a specially constructed room provided with forced ventilation. Despite the magnitude of ventilation the concentration of gasoline vapor was high enough to be immediately disturbing to one who was not accustomed to such vapor. In addition, the skin, clothing and shoes of the workmen were frequently and almost continuously wet with gasoline. The barrels were lined up in a double row along corresponding rows of pipe lines each of which was provided with an elbow, a flexible hose and a float valve. Each hose line with its valve was inserted into a drum, and the valve was opened. Gasoline flowed in at considerable pressure until the level of liquid in the drum released the valve, thus closing it, Occasionally the valve refused to work properly, at which time a stream of gasoline rose from the drum and thoroughly drenched any workmen in its immediate vicinity.

The number of men engaged in filling and handling the drums of gasoline was small but the severity of exposure was such as to give excellent opportunity for the detection of any effects which might result from gasoline absorption. These men were carefully examined in a manner which will be described later, and several types of laboratory data were obtained, including the lead content of the urine and feces. (The latter data were obtained because of our interest in the lead excretion of groups of workmen with no occupational exposure to lead compounds.)

Shortly after these examinations had been completed the refinery in question undertook the distribution of leaded gasoline. The latter was handled in the manner described above for ordinary gasoline. Inasmuch as experimental evidence indicated that the hazards of lead absorption from skin contact and inhalation of vapor from gasoline containing tetraethyl lead were practically negligible, no fears were entertained as to the consequences of the additional factor of a low concentration of tetraethyl lead. Nevertheless, this constituted a unique severity of exposure. Therefore it was considered advisable to obtain information which would show whether or not the men were absorbing lead. Accordingly, at the end of a period of 6 months, during which leaded gasoline had been handled daily in the previously described manner, the workmen so employed were examined, and samples of their excreta were obtained for analysis. In this second group, made up of 22 men, there were ten who had been included in the first set of examinations.

Except in the case of the barrel-fillers, comparable groups of subjects unexposed to the potential dangers of leaded gasoline, were not obtained for study. At the time of the study there was no area of the United States in which the selection of entirely unexposed subjects could be made, since the use of leaded gasoline had increased so as to involve all parts of the country. Therefore it was necessary to rely on information obtained prior to the general distribution of leaded gasoline, for comparative data on similar groups of subjects independent of this factor. On the other hand, since repeated observations had been made on the same individuals under conditions of continuous exposure, the successive findings furnished a means for the discovery of progressive effects of any type.

Experimental Methods.

Experimental studies on animals and men have established the existence of a relationship between the magnitude of the lead exposure and absorption and the rate of lead excretion, in that fecal excretion is a measure of ingestion on the day preceding the collection of the sample, while the urinary excretion indicates the magnitude of lead absorption (6, 7, 8). Nevertheless, we wished to leave no stone unturned which might yield additional information. Accordingly we searched for clinical evidences of lead absorption with the same care that we applied to the collection of accurate analytical data.

Care was taken to obtain all the information possible from each subject, and to record such information in an uniform manner. For this reason cards for recording data were provided as reproduced in Figures 1 to 5 inclusive, and the work was divided among four physicians each of whom carried out the same type of observations on each subject. So far as possible quantitative information was obtained in the physical examination, but without the subordination of clinical judgment. Thus while it was recognized that a statistical study of all the data was desirable, clinical diagnostic methods as applied to individual cases were regarded as of greater importance in determining whether or not any evidence of lead intoxication had appeared among the subjects. As an example of this point of view, each subject was tested for evidences of atrophy or muscular weakness by palpation and by opposing the examiner's strength to that of the corresponding muscle group of the subject. But for the purposes of statistical comparison of a single neuro-muscular factor, the grip was tested by a hand dynamometer. (The same instrument was employed throughout the tests.) Measurements of the blood pressure of each subject (seated) were made with a standard manometric apparatus. A fresh specimen of urine was obtained from each subject and examined at once for its reaction, the presence of albumin, and sugar. Microscopic examination of the urine and a test for acetone were carried out only when indicated by chemical abnormalities or by suggestive clinical findings. Erythrocyte, leucocyte and differential leucocyte counts were made as ~~a~~ routine procedure only on the barrel-filler group of subjects. Otherwise, such procedures were followed only when indicated for diagnostic purposes. Hemoglobin determinations were made on each subject by means of the Dare hemoglobinometer. A single instrument was employed for all observations, and all readings were made by the same observer. Blood smears were made on all subjects, and were examined for stippling of the erythrocytes by a standardized method which will be described elsewhere by L. W. Sanders.

Samples of urine and feces were obtained from the subjects for the determination of their lead content. The collection of these and the analyses were carried out according to methods which we have described previously (9). In a few instances no samples were obtainable. A further small number of samples were lost in transit and in process of analysis. With these few exceptions, the analytical results were obtained without difficulty.

4. Experimental Findings.

No case of lead intoxication was found among the subjects. In fact, no combination of symptoms and physical findings was suggestive of lead intoxication. Such evidences of lead absorption as are common among lead workers were conspicously absent. Of special negative clinical importance were the complete absence of lead line, the lack of significant microscopic blood changes (stippling), and the infrequency of vague symptoms of ill health. Under these circumstances any evidences of significant lead absorption as a consequence of exposure to leaded gasoline must be sought in the data on the excretion of lead.

Certain of the clinical findings and all of the analytical data for the groups are presented in a series of tables which represent the exact manner of the statistical study except as otherwise noted. Numerous other clinical items which were subjected to statistical analysis, have been omitted because of their negative significance, and for the sake of brevity.

Table 5 shows the classification of the subjects according to the duration of their exposure to leaded gasoline. One-half of the filling station attendants and a little less than half of the tank wagon handlers had been exposed for 5 years or more, while 69 per cent of the garage mechanics had repaired cars which used leaded gasoline over a period of 3 years or more.

Whether or not it has any bearing on the problem at issue, the occurrence of previous industrial lead exposure among the subjects may not be ignored. Information on this point obtained from the occupational histories is shown in Table 6. Here it may be seen that a large proportion of the subjects had been employed in trades which involved some opportunity for lead absorption, prior to their exposure [illegible] of the garage mechanics may be regarded as from the factor of leaded gasoline. However, it may be assumed that few garage mechanics have more than a slight lead exposure in the course of their normal day's work, since small jobs of soldering and painting and the occasional repair of a storage battery have not produced a noticeable occurrence of lead intoxication among garage mechanics . One tank wagon driver and 8 garage mechanics had been employed at some previous time in hazardous lead trades, in which their exposure had not been severe either in quality or duration.

The distribution of the subjects according to age, seen in Table 7, is significant only in that it demonstrates the inclusion of widely varying age groups among the subjects under investigation.

In Tables 8 and 9, the findings as regards haemoglobin of the blood, and stippling of the erythrocytes are recorded. No mean values were computed for the occurrence of stippling by reason of the high proportion of negative results. It may be seen from the tables that no significance may be attached to variation in these matters in relation to leaded gasoline exposure, since practically all the findings are within normal limits. However there is a high frequency of low hemoglobin readings and of abnormal numbers of stippled erythrocytes among the barrel-fillers exposed to ordinary gasoline. These men were examined in the summer when inhalation of gasoline vapor was at its height. Apparently, exposure to gasoline vapors may produce blood changes, including the appearance of stippling.

The facts obtained from the analysis of the excreta of the subjects are presented in Tables 10, 11, and 12. A survey of the tabulated results shows that a few high results are scattered irregularly through the data. Where these occur in fecal smaples it may be assumed that they have resulted either from contamination of the sample or from the ingestion of unusual amounts of lead with food material, and that they have no necessary or probable relationship to occupational lead exposure. The inclusion of such findings in the computation of mean values increases appreciably the probable error of the mean, and militates against satisfactory comparison of the groups of subjects. Nevertheless, such results have been recorded, and have been included in the calculations unless otherwise specifically noted in the tables. Where a result has been excluded it has been for the purpose of eliminating a finding which has no probable relation to the problem at issue. In the case of the urine samples, aberrant results are of rare occurrence, as would be expected. On the other hand, contamination of an occasional sample during the process of collection is apparently unavoidable, despite the most careful instruction of the subjects. This is not remarkable when the ubiquity of lead compounds is appreciated, and when the lack of understanding of chemical cleanliness on the part of the subjects is taken into account.

The analytical results serve to classify the various groups of subjects as distinctly outside the hazardous lead trades. (Compare with data from certain lead trades (6)). At first glance, the mean values for the lead content of the feces of filling station employees, tank wagon handlers and garage mechanics seem high, as compared to those for normal persons with no occupational lead exposure. On the other hand, the small group of barrel fillers who were not exposed to leaded gasoline, and who had no other occupational lead exposure at the time of the examination, show similarly high findings. Furthermore, when the fecal lead is expressed in quantitatively comparable terms, (in milligrams per gram of ash), the apparently high results lose their significance. Finally, for reasons which we have pointed out elsewhere (8) it is impossible to draw exact conclusions as to the magnitude of lead absorption, from the results obtained on samples of feces, and it is necessary to resort to the study of the urinary excretion for such information. As judged by this standard, the groups fall into the category of persons lacking occupational exposure to lead compaunds.

A special significance is attached to the failure of the barrel fillers to show any increase in their lead excretion as a consequence of their exposure to leaded gasoline. Not only do the two groups fail to differentiate themselves from the point of view of lead excretion, but it is equally true that no single individual in the groups can be differentiated. Of the 10 persons who were examined prior to exposure to leaded gasoline, and again after 6 months exposure to leaded gasoline, no person shows an increase in his rate of lead excretion. This can be interpreted only as meaning that there was no significant lead absorption as a consequence of this exposure. Thus, it seems quite clear, that the inability of animals to absorb measurable amounts of tetraethyl lead out of gasoline in dilute solution (5), (1 part per 1000 by volume or less) is shared by man.

5. Comparison of the Findings with Results Obtained Earlier.

In view of the importance of the conclusions of the above paragraphs, indicating the negative character of the findings, it is proper to present observations of a comparable character on groups of subjects similar in every matter save that of exposure to leaded gasoline. Accordingly, Tables 13 to 18, inclusive, show results obtained in 1927, in a study of groups of persons who had not been exposed to the conditions associated with the use of leaded gasoline. The medical student group is composed of members of a newly matriculated class. For the second group, filling station attendants and bulk handlers of ordinary gasoline are combined in order to make a large group for statistical purposes. Unfortunately, no analytical data are available in the case of the bulk handlers of gasoline, because of their unwillingness to provide us with samples of their excreta, and therefore the analytical findings relate only to filling station attendants, as indicated in the tables. The control garage mechanic group is made up of only a small number of men carefully selected in 1926 as lacking any exposure to leaded gasoline. The rigid requirements in the latter regard introduced considerable difficulty into the problem of obtaining cooperative subjects.

No explanatory comments are required, since the tables present the observed facts adequately. It should be pointed out that the observations recorded in these tables were made by the same persons who collected the data on the exposed subjects previously described. The clinical methods employed in the two instances were substantially the same, while the analytical methods were practically identical.

Table 19 summarizes the mean values for all the groups of exposed and unexposed persons, in such matters as would seem to have special significance. (Since the frequencies of occurrence of stippling do not lend themselves to computation of mean values, comparison of this important factor must be made from the tables of distribution.) Comparison of the means reveals a lack of statistical differentiation of the groups. The medical students show a significant difference in age, but in no other factor. The barrell fillers not exposed to leaded gasoline show a significantly low hemoglobin content of their blood, as previously pointed out. The mean lead content per sample of feces also shows certain statistically significant variations within the groups, but no actual importance can be attributed to these differences in view of the variability in the size of the fecal samples. When the latter factor is corrected by expressing the lead in the feces in relation to the quantity of ash, the variability of the groups is statistically insignificant.

The Influence of Previous Occupational Lead Exposure.

It has been intimated that some significance may be attached to the fact that a considerable number of the subjects had been exposed to lead compounds in previous occupations. Likewise the handling of lead compounds other than those associated with leaded fuel, might be expected to have some influence upon the lead absorption of the garage mechanic. As a means of ascertaining the importance of these matters, the analytical results derived from two small groups of persons whose occupational histories failed to give evidence of previous lead exposure, were subjected to study. (Table 6 has shown the distribution of the subjects as to previous occupational lead exposure.) Table 20 presents the mean values for the lead excretion of these subjects as separate groups and in combination. The results are seen to be slightly lower, but no significant statistical differences have resulted from the exclusion of the previously exposed subjects.

Lead Excretion in Relation to Length of Exposure to Leaded Gasoline.

An examination into the relationship between length of service and lead excretion, might provide a means of ascertaining the significance of the lead exposure associated with the occupation of the garage mechanics. This was done by studying the correlation between the magnitude of lead excretion and the period of continuous employment as mechanics, and then by a corresponding study of the magnitude of lead excretion in relation to length of exposure in repairing cars which used leaded gasoline. The results of these attempted correlations are shown in Table 21. There is a complete lack of correlation in either matter. From these results one must conclude either that the lead exposure associated with the occupation is insignificant, or that it is of such irregular occurrence as to have no measurable time relationship.

There remains one other means of examining the available data in search of evidences of lead absorption from the handling of leaded gasoline. Among the subjects studied in 1929, there were 26 filling station attendants, and 24 tank wagon handlers who had been employed as subjects in 1927. Presumably, if their occupation contained a significant lead hazard they should show some evidence of change in lead excretion after 2 years. The findings for the two years, as to lead excretion, are shown in Tables 22, 23, and 24. The mean values are summarized in Table 25. No statistically valid difference is demonstrable.

6. Summary and Discussion.

Three hundred and one men who had incurred the severest and longest exposure to leaded gasoline and its combustion products were studied as to their physical fitness and their lead excretion, during the winter months of 1929-30. No clinical evidences of lead absorption or of lead intoxication were found in any individual, and no indication of lead absorption, as a consequence of the exposure, was detected when the subjects were compared as to their lead excretion with corresponding groups of unexposed persons who had been studied previously. Moreover there was no measurable change in the lead excretion of a group of fifty of the subjects who had been studied in a similar manner in 1927.

The lead excretion of a number of workmen was determined before and after a 6 month period of intense skin exposure to leaded gasoline. No individual in the group showed an increased lead excretion following the period of exposure.

The level of human lead excretion has been shown to be highly sensitive to the magnitude of lead exposure and absorption (6,8), and since the subjects failed to show an increase in their lead excretion, it is apparent that little exposure to lead existed, and that no significant absorption of lead occurred. In view of our previously published findings as to the lead absorption and excretion of unexposed persons (3,9), it must be recognized that the magnitude and variability of lead ingestion with food is sufficient to mask a slight lead absorption which may result from exposure to the conditions arising from the use of leaded gasoline. If this has occurred, the relative insignificance of the contribution made by leaded gasoline to the total lead absorption of the experimental subjects is obvious. On the other hand, the technic employed in the foregoing observation should be modified so as to control the factor of individual lead ingestion on the part of exposed persons, if the precise magnitude of the occupational lead exposure is to be measured. We shall present the results obtained through the use of the latter method of study in a subsequent article.

In view of the negative evidence obtained in this study of persons whose exposure to leaded gasoline and its combustion products was magnified to a point well above that which is possible in the general population, there is no reason to fear the existence of danger to the public health from the distribution and use of leaded gasoline.

7. References

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TABLE I.

Period Of Distribution of Leaded Gasoline in Various American Cities Up to October 1929

Locality	Date of First Distribution		Interval of Discontinuance	Years of Continuous Distribution
Dayton, Ohio	February	1923	none	6.7
Cincinnati, O.	April	1923	none	6.5
Wheeling, W. Va.	Summer	1923	May 1925 to summer 1926	3.2
Chicago, Ill.	Autumn	1923	" " " " "	3.2
Detroit, Mich.	Autumn	1923	" " " " "	3.2
St. Louis, Mo.	Spring	1924	" " " " "	3.2
Kansas City, Mo.	Spring	1924	" " " " "	3.2
Minneapolis, Minn.	Spring	1924	" " " " "	3.2
Milwaukee, Wis.	Spring	1924	" " " " "	3.2
Baltimore, Md.	Spring	1924	" " " " "	3.2
Washington, D. C.	Spring	1924	" " " " "	3.2
San Antonio, Texas	Spring	1924	" " " " "	3.2
Savannah, Ga.	Autumn	1924	none	5.0
Atlanta, Ga.	Autumn	1924	"	5.0
Jacksonville, Fla.	Autumn	1924	"	5.0
New Orleans, La.	Spring	1926	"	3.2
Cleveland, Ohio	Summer	1926	"	3.2
Philadelphia, Pa.	Summer	1926	"	3.2
Boston, Mass.	Summer	1926	"	3.2
Denver, Colo.	Summer	1926	"	2.2
Spokane, Wash.	Summer	1926	"	2.2
Tulsa, Okla.	Summer	1926	"	2.2
San Francisco, Cal.	Winter	1926	"	2.2
Los Angeles, Cal.	Winter	1926	"	2.2

Approximate Gross and Comparative Consumption of Leaded Gasoline in Various Areas of the United States From 1926 to October of 1929

	1926		1927		1928		1929 (9 mo)	
Distribution Areas of the United States	Millions of Gallons of Leaded Gasoline	Percent of Leaded Gasoline to Total Gasoline	Millions of Gallons of Leaded Gasoline	Percentage of Leaded Gasoline to Total Gasoline	Millions of Gallons of Leaded Gasoline	Percent of Lead. Gas. to Total Gasoline	Millions of Gallons of Leaded Gasoline	Percent of Leaded Gas. to Total Gasoline
New England States and New York	11.9	0.8	54.8	3.1	[illegible]	4.6	90.3	5.2
Pennsylvania	7.9	1.4	31.7	4.6	73.9	9.7	82.1	12.1
Atlantic Coast States	10.3	0.9	5.8	0.4	15.8	1.2	90.3	8.2
Ohio	1.6	0.2	17.3	2.3	89.7	10.4	147.8	20.5
Kentucky Georgia Florida Miss., and Alabama	4.8	0.6	20.2	2.5	36.9	4.3	49.3	7.2
Louisianna Arkansas Tennessee	0.8	0.2	0.3	0.07	10.6	2.3	49.3	13.2
Central States	36.5	1.2	112.5	3.2	163.6	4.1	238.2	7.1
Texas Oklahoma	1.6	0.2	2.9	0.3	5.3	0.6	16.4	2.0
Rocky Mt. States	4.0	1.4	11.5	3.4	15.8	4.0	16.4	4.9
West Coast States	0.0	0.0	31.7	3.3	26.4	1.7	41.1	3.2
TOTAL	79.4	0.8	288.8	2.4	527.8	4.1	821.3	7.4

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TABLE # 3

Average Tetra-ethyl Lead Content of Gasoline in Various Areas of The United States from 1926 to 1929

Distribution Areas of United States	Average Tetraethyl Lead Content in Cubic Centimeters per Ga			
	1926	1927	1928	1929
New England States and New York	1.4	1.1	1.2	0.9
Pennsylv nia	1.2	1.0	1.2	1.65
Atlantic Coast States	1.7	1.6	1.4	1.5
Ohio	0.9	1.2	1.1	1.5
Kentucky, Georgia, Florida, Miss. and Alabama	1.0	1.7	1.7	1.9
Louisianna, Arkansas and Tennessee	0.9	0.6	0.9	1.3
Central States	1.4	1.6	2.2	2.0
Texas and Oklahoma	1.4	1.7	2.0	2.7
Rocky Mountain States	1.3	2.0	2.4	2.4
West Coast States	-	0.7	1.5	1.5
United States as Whole	1.4*	1.6*	1.75	1.62

* These figures are estimates only and may be somewhat in error.

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