STANDARD OIL COMPANY OF CALIFORNIA

L. E. CURTIS, M. D.
MEDICAL DIRECTOR
JAMES RYAN, M. D.
ASSISTANT MEDICAL DIRECTOR
225 BUSH STREET
SAN FRANCISCO 20, CALIFORNIA

August 24, 1962

RICHARD DILLON, M. D.
REGIONAL PHYSICIAN
605 WEST OLYMPIC BOULEVARD
LOS ANGELES 54, CALIFORNIA

METHYL STUDY
131.31

Robert A. Kehoe, M. D.
c/o Mr. Harold Greer
P. O. Box #206
Steamboat Springs, Colorado

Dear Bob:

Very sorry about the misunderstanding regarding the copy of report you sent me and Dr. Princi's articles for publication. I also wish to apologize for the condition of this report which I am returning herewith, but numerous people participated in the study and evaluation of it.

Naturally, many of the comments that I make will be similar or identical to the ones made regarding Dr. Princi's report.

Page 3, Line 4. I would like to point out that the absorption of lead is not revealed by measurement of lead in the urine; rather, the excretion of lead is so measured.

Page 4, Line 5. This sentence, in order to be accurate, must be reworded somewhat as follows: "All of the men engaged in blending, gauging, filling and doing quality control work where there was potential exposure at the refinery in the San Francisco area were investigated." The designation of San Francisco or Los Angeles refinery should be clarified throughout the report to be San Francisco area or Los Angeles area.

Page 5, Paragraph 2, Line 4. We suggest this be changed to read ".....established clearly the sites at which the greatest exposure to the vapor of gasoline might occur. Those who were employed regularly as 'loaders' were included in the investigation."

Page 5, Paragraph 3, Line 5. We suggest deleting "exposure" and substituting "a possibility." The way it is now worded, it indicates that the men were exposed and this is not necessarily a true conclusion.

Page 6, Paragraph 1, Line 7. We suggest deleting "severe and regular" inasmuch as, insofar as we know, both before and after the

investigation, no men were subjected to severe and regular exposure.

Page 7, Paragraph 2, Line 8. We suggest changing the term "technologist" to "hygienist" and deleting "in the Medical Department" inasmuch as, organizationally, industrial hygienists do not report within the Medical Department.

Page 10, Line 5. I assume you will catch this typographical error but, in case you don't, it should read "tetramethyl lead" instead of "tetraethyl lead."

Page 14, Paragraph 3, Line 4. We suggest, to clarify the meaning, this be worded "The applications of the two methods to each of two duplicate samples" if this is what was done. Otherwise, it should be reworded to make it clear just what the procedure was.

Page 15. This table lumps all samples containing lead indicating concentrations greater than five micrograms per cubic foot at the dome of tank cars as one figure with the individual values given below. Since the mean of the total number of samples in this column falls in the highest range shown, it appears that a more representative display of data is called for.

Page 17. We suggest it would be simpler reading if the same system of reporting, that is "micrograms per cubic foot" or "micrograms per cubic meter", were used throughout the report or, if you prefer, both methods could be utilized in the chart.

Pages 31 and 32. It is not true that the physicians responsible for the exercise of clinical critique were apprehensive during the early weeks of the investigation since we were completely convinced by the animal studies and by the laboratory studies that there would be no severe hazard with this material. The work with the Taxicab Company convinced us completely that there was no particularly greater hazard than with the use of tetraethyl lead. True, we asked for immediate reports on the analyses of blood and urine, but that was done more out of interest in the study than because of any particular concern regarding the hazards, nor did we "relax" into the routine of collecting samples. Insofar as the final examination was concerned, you will recall I discussed this matter with you and you agreed it would be satisfactory to perform only our routine examinations and it was not necessary to do the full history and physical examination which was done at the beginning. Later, chest X-rays were requested and obtained for you. Inasmuch as you were directing the work you wanted done and we were willing to cooperate, I feel, if there is any criticism of the final examination, it should be directed at yourself rather than at this medical group.

Page 52. Summary 1 (a), Line 2. I suggest you delete "...in the areas in which the antiknock compound is mixed with gasoline" since this is not true nor is it supported by the findings. Deleting this will give a more factual picture. In the last line of the page, we suggest substituting "dome area" for "these points."

Page 53, Line 3. We have been unable to correlate these figures with those given in Tables 1 and 2 and suggest they be re-examined.

Page 56, Line 5. All the tests covered a period of one year and many a period up to 16 months, rather than the 9 months you have indicated here.

Insofar as credits are concerned, we suggest the addition of Dr. Lawrence A. Gerlach of DuPont and Mr. John F. Koehnle of Ethyl Corporation.

Sincerely yours,

L. E. CURTIS, M. D.

LEC:mr

Enclosure

There were two sites one in each of the refineries in which the concentrated product was being mixed with gasoline. The conditions under which such work is done provide little opportunity to the workmen for exposure to tetramethyllead, but the potentiality was worthy of investigation. All of the men in one of the refineries (S.F.), were investigated.

In one refinery (S.F.), but not in the other, there was a technical laboratory in which the work was of such type and scope as to justify investigation.

There was also, in one refinery (S.F.), a facility for filling barrels with gasoline, some of which would contain tetramethyllead. This operation was being conducted under such conditions and with such equipment as to minimize the exposure of the workmen to contact of their skin and clothing with gasoline, or to the inhalation of vapors. Moreover, this work was done intermittently, there being only a limited demand for gasoline in such containers, and only a modest proportion of that so marketed contained tetramethyllead. Five workmen, only, of which two comprised the regular crew, were engaged in this operation as required.

From this same refinery shipments of gasoline were made by sea, and on a long wharf were men who loaded, inspected and gauged such cargoes in tankers and barges. Four men were engaged more or less regularly in operations in which gasoline containing tetramethyllead was involved, and these came naturally under observation in this relationship.

Five men in the refinery in the Los Angeles area were

engaged, regularly, among other duties, in gauging the gasoline in storage tanks.

At a single site in each of the two refineries men were employed in filling tank trucks with gasoline (the larger number in the San Francisco area). Critical observation in and around these sites established clearly the sites at which the ~~men were subjected to the most severe and most prolonged exposure~~ greatest exposures to the vapor of gasoline, ~~and also demonstrated that~~ those who were employed regularly as "loaders", were ~~obviously the subjects~~ selected for investigation. These men, 10 from the one (S.F) and 3 from the other (L.A.), were selected for examination. (Approximately 80 drivers of tank trucks were excluded, after a careful consideration of their manner of handling gasoline at various destinations, in view of the relative insignificance of their potential exposure.)

In the consideration of the sites, referred to above, and of the workmen employed thereat, there was no semblance of random selection. These were the only sites in the refineries at which there was the potentiality of exposure to tetramethyllead, and these were the men who were subjected to such ~~exposure~~ exposures. The recognition of positive evidence of the effects of exposure upon workmen, by comparison with similar observations made in the absence of such exposure, could be made broadly on the background of comparable information obtained in prior years in the investigation of persons engaged in the handling of gasoline containing tetraethyllead. It could also be sought on the basis of any change which might occur in these individuals, as they were investigated from time to time over the total period of the observations.

The process of the selection of sites and subjects (employees) from among the large number of widely scattered service stations in the two major areas (and one in Bakersfield) of the distribution of gasoline containing tetramethyllead differed appreciably from that described above. Here again, however, the effort was made deliberately to seek out the more severe environmental conditions afforded within the two areas, and within these to select the men whose work involved the ~~most severe and regular~~ exposure to gasoline containing tetramethyllead, and where employment would be the least likely to be terminated within the period of the investigation. The specifications for selection in both instances were relatively simple, involving, for the sites, (a) a fairly wide georgraphic distribution, and (b) a comparatively large sale of gasoline containing tetramethyllead to customers; and for the workmen, (c) continuity of employment in the regular duties of service station attendants. As to the latter qualification, there is an appreciable turnover of employment among service station attendants, except for the manager and the assistant manager; these tend to be on the job daily and to continue in their employment for considerable period of time.

In accordance with these general specifications, a selection was made of service stations according to the volume of leaded gasoline dispensed, and on this and the geographic basis, 10 in each of the two major areas, involving the 28 most likely men (San Francisco), and 32 in the other (Los Angeles), were listed as subjects for detailed observations. Three additional men, at a service station in Bakersfield, were included.

Two sites, one in the most centrally located area of San Francisco,

and the other in a roughly corresponding part of Los Angeles (the differences in the extent and topography of the two cities are striking) were employed for the sampling of the ambient atmosphere (for general information and comparison with the other sites of sampling). The equipment was situated on the roof of a four-story clothing store in down-town San Francisco, and on the roof of a two-story business building in Los Angeles. Both of these sites were such as to provide apparently unobstructed access to the ambient air without any risk of involvement in any visible or otherwise demonstrable plume (or plumes) of smoke or fumes from nearby stacks.

Investigative Procedures and Methods

In view of the fact that all of the premises in which environmental conditions and workmen were to be investigated were the property of Standard Oil Company of California, and that the workmen were employees of the Company, plans had to be made through appropriate representatives of this Company for the proper conduct of the observations. The physicians of the Medical Department of the Company were responsible for the medical supervision (in occupational matters) of the employees, and an industrial ~~technologist in the Medical Department~~ had supervisory responsibility for the environmental conditions under which the men carried out their work. It was essential that these professional relationships should not be attenuated or abridged in any manner by the investigative procedure, and accordingly, all aspects of the investigation had to be worked out with these matters in mind. The medical examinations

and the collection of samples of urine and blood were delegated to these representatives of the Company, after a detailed discussion of the procedures to be employed, and the records to be obtained. The containers for the samples of urine and blood were supplied, however, by the Kettering Laboratory, and the procedures involved in collecting the samples were prescribed by the Laboratory. As we shall have occasion later to note, the decision that the medical examinations should be so handled resulted in some loss of detailed information for the record, in that the final medical examinations, made somewhat more than a year after the first series, were not carried out in precisely the initial manner nor with complete coverage of all of the individuals. This lack of information is not as significant in the practical, however, as it is in the experimental (documentary) sense, since the relationship between these physicians and the employees under their supervision is of a type that provides every reasonable guarantee that no illness or complaint escapes medical attention.

Aid in the performance of some of the manipulations of the investigation was provided by technical representatives of Ethyl Corporation (in the Los Angeles area) and of E. I. du Pont de Nemours and Company (in the San Francisco area), who also participated in the conferences in which the methods of procedure were discussed in detail and delegated to various individuals and groups. The distance between the Kettering Laboratory and the sites of the observations, together with the availability on the West Coast, of competent technical personnel of the two industrial organizations, led the staff of the Laboratory to welcome such fully coöperative and reliable assistance. The sites were visited, however,

by the representatives of the Laboratory, and explored thoroughly for their suitability, and for their yield of satisfactory and representative personnel. Easy and frequent communication between the Laboratory and those who participated in this manner in the investigation, enabled the work to be carried out with an economy of effort and a dispatch that contributed appreciably to its efficiency.

On two occasions, some weeks apart, all participants in the investigation assembled for the purpose of considering and planning the investigation, so as to arrive at comprehensive and essentially uniform methods for the atmospheric sampling, as well as the examination of personnel, and the collection of samples of urine and blood in containers supplied by the Kettering Laboratory. The first of such conferences dealt with the general problem in a comprehensive manner, with the general design of the investigation, and with the specific tasks which were to be undertaken by the collaborating groups and individuals. The second brought forth a final draft of a protocol in which the instructions of the Kettering Laboratory with respect to the types and frequency of the collection of samples from the air, the details of the operation of the equipment, the preparation of certain samples for shipping, and all other pertinent procedures were set down. Forms for recording the medical findings were also adopted, and a schedule supplying containers for samples of urine and blood, for returning these and other samples to the Kettering Laboratory, and for reporting and recording the findings, were agreed, upon.

Methods of Environmental Sampling and Analysis

Organic lead in the air at various sites was determined by means of equipment designed for the purpose and tested by a considerable period of use in the field.* The rate of flow of air into the iodine scrubbers (2 in series) was 0.25 cu.ft. per min. - relatively slowly - to allow for the effective quantitative removal of ~~tetraethyllead~~ from the air, as compared with that required for the quantitative removal of tetraethyllead. The lead retained in each of the two scrubbers was determined directly in the field, the sum of the two results yielding the total quantity of organic lead found in the volume of air sampled. In sampling the air at the various sites within the refineries, the volume of air sampled was 4 cubic feet. This volume was also drawn through the wash bottles at gasoline service stations initially, but was then amplified to 8 cu.ft., as a rule, and occasionally, as circumstances dictated, to 12 or even 16 cu.ft., in order to obtain adequate quantities of organic lead when the concentration in the air was too low for accurate determination otherwise.

At the ~~filling~~ stations (where it was essential to remove particulate lead compounds from the air before it entered the scrubbers in which organic lead was to be collected), the air passed through type AA Millipore filters (37 mm. in diameter with pores 0.8 micron in diameter). A specially constructed holder for the filter and scrubbers (see Fig.1), and a Gast air pump (1 cfm in capacity), were furnished to each group by the Kettering Laboratory. The holder could be held in the hand, fastened to a rod on a stand, or hung over the window of an

* Snyder, L.J. et al: Determination of lead in air. Rapid micro-method for field use. Anal. Chem., 20:772, 1948.

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Fig 1.

automobile, while the air was being sampled. Suction could be obtained by means of the Gast pump, or by the hand pump of the special sampling kit. The organic lead in the wash bottles was determined in the field, but the Millipore filters were returned to the Kettering Laboratory for the determination of their content of inorganic lead by a procedure outlined in Appendix 1.

The concentration of lead in the atmosphere of a commercial area in each of the two cities (Los Angeles and San Francisco) was determined by the analysis of material collected on filter webs of fiber glass employed in Staplex high-volume samplers as supplied by the Kettering Laboratory. The particulate material was removed from about 2000 meters of air by each filter during each period of 24 hours of sampling. After use, these webs were shipped to Cincinnati, where they were analysed for their content of lead by a spectrographic method developed in this Laboratory. *

The following schedule of sampling was adhered to:
The installation in the refinery in which the concentrated antiknock fluid was mixed with gasoline, and the loading racks at the two refineries, were visited initially every other week, and later at convenient times. Other samples in the refineries (from laboratory, wharf, and the barrel filling operation) were collected as opportunities were afforded when gasoline containing tetramethyllead was being handled. Samples collected at these operations were analyzed for their content of organic lead only.

*Cholak, J. and Story. R.V.: Spectro-chemical determination of trace metals in biological material. J. op. Soc. Am. 31:730,1941.

Each ~~filling~~ service station was visited for sampling at least once each month. During any one visit, 1 to 3 samples, depending on the activity, were taken. These samples were analyzed for their content of both inorganic and organic lead compounds. The carbon monoxide content of the air was also determined during each visit. Bureau of Mines indicator tubes were used for this purpose.

Samples of particulate material in the atmosphere at the two central locations in San Francisco and Los Angeles, were collected every other day, and were analyzed for their content of inorganic lead. (Adequate evidence has demonstrated the futility of the search for organic lead in the atmosphere of such areas.)

Methods for the Investigation of Personnel

Each individual in the several groups of employees was examined by a physician. The examination consisted of an occupational and medical history, a complete physical and hematological survey, and certain other laboratory procedures of a routine or specialized nature, e.g., x-ray films, according to the schedule of the Medical Department in such matters, augmented by the judgment of the physicians. At the initial examination, dupplicate samples of blood (in some instance only one) for analysis for lead were obtained from each man, together with a specimen of urine of small volume (a single voiding), collected in containers supplied by the Kettering Laboratory in accordance with the instructions of the Laboratory. All of such samples were forwarded to the Kettering Laboratory for analysis, after having been suitably labelled for identification.

The first series of samples of urine and blood were collected in June and July, 1960; additional samples of urine were collected from

each man (with only a few exceptions) at intervals of approximately 90 days, while the fifth and terminal samples of urine, and the second and final samples of blood, were collected in July and August, 1961.

The specimens of urine were analysed by a method which has been in use in this Laboratory for many years, with such slight improvements in technique as have been shown to contribute to its precision.*

The analysis of the blood was carried out by two methods, one a colorimetric method with dithizone, referred to above, and the other a spectrographic method,* also developed in this Laboratory. The application of the two methods to duplicate samples carried through the analytical procedures by different analysts, has the combined virtues of checking the analytical work, and of detecting the infrequent but disconcerting occurrence of the contamination of a specimen of blood during its collection, transportation and handling in the laboratory.

Results

Environmental Findings

1. At the Refineries.

The frequencies of occurrence of the various ranges of the concentration of organic lead in the air at the several locations in the two refineries, together with the mean levels of concentration (and the deviations), are assembled in Tables 1 and 2. It will be noted that these data, as are all of those in this section of this report, with

* Cholak, J., Hubbard, D.M., and Burkey, R.E.: Micro determination of lead in biological materials. With dithizone extraction at high pH. Anal. Chem., 20: 671,1948.
Cholak, J., and Story, R.V.: Spectrochemical Determination of Trace Metals in Biological Material.

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Table 1

The Frequencies of Occurrence of Various Levels of Concentration of Organic Lead in the Air, Within the Ranges Indicated, at Certain Locations in a Refinery in the San Francisco Area

Ranges mic.g. per cu.ft.	In Blending Area			At Loading Racks		Barrel Filling Area	Inspection Laboratory on Wharf	In Chemical Laboratory
	At Dome of Car	At Weigh Tank	Outside	On Top of Truck	On Ground			
0.- 0.49	5	19	4	16	22	3	3	30
0.5 - 0.99	11	6	14	27	8	-	1	
1.0 - 1.49	6	2	2	10	1	-		
1.5 - 1.99	5	1	6	8	1			
2.0 - 2.49	0	0	3	1				
2.5 - 2.99	2	1	2	4				
3.0 - 3.49	4							
3.5 - 3.99	3							
4.0 - 4.49	2							
4.5 - 4.49	34		1					
5.0+	11 13*							
Number	59	29	32	66	32	3	4	30
Mean	4.63	0.32	1.13	0.58	0.27	0	0.13	0
Std. Dev.	6.41	0.57	1.30	0.64	0.80			

* 6.0, [illegible], 12.0, 5.2, 15.0, 10.0, 10.0, 15.0, 13.0, 6.0, 6.5, 5.0, 6.5, 35.0, 26.0, 6.0, 16.5, 5.0

Table 2

The Frequencies of Occurrence of Various Levels of Concentration of Organic Lead in the air, Within the Ranges Indicated, at Certain Locations in a Refinery in the Los Angeles Area.

Ranges mic.g. per cu.ft.	Blending Area			Loading Rack	
	At Dome of Car	At Weigh-Tank	Ground Outside	Top of Truck	Ground Level
0.0 - 0.49	7	9	19	6	4
0.5 - 0.99	3	7	2	6	7
1.0 - 1.49	2	5	1	5	4
1.5 - 1.99	2	1	1	0	3
2.0 - 2.49	2	0	-	2	1
2.5 - 2.99	0	1	-	1	0
3.0 - 3.49	1	0	-	0	0
3.5 - 3.99	0	0	-	0	1
4.0 - 4.49	3	1	-	1	1
4.5 - 4.99	0	0	-	0	0
5.0*+	5	0	-	0	0
Number	25	24	23	21	21
Mean	2.91	0.86	0.18	0.98	1.12
Std. Dev.	3.56	0.94	0.38	1.00	1.01

the exception of those in Table 8, to which reference will be made later, are expressed in micrograms per cubic foot, the reason being that they were obtained in this form because of the design and calibration of the equipment employed. They can be converted to the more familiar form of micrograms per cubic meter of air, by multiplying the recorded values by 35.3 (the number of cubic feet in a cubic meter), but it has seemed best to report them as they were observed.

Comparatively high concentrations of organic lead were found, as expected, in proximity to the domes of tank-cars used for the transportation of the concentrated antiknock compound, when their domes were first opened and connections were made with the pipe lines leading to a weigh-tank within the building in which the mixing equipment was housed, in preparation for the unloading of the tank-car. The variability of the results obtained at one or the other of the two sites, as well as the variation between the two sites, depended upon the condition of the interior of the domes, and that of the valve connections, as well as the precise time of the sampling in relation to the stage of these operations, and the actual point of sampling. The generally higher values obtained in the San Francisco refinery are attributed mainly to the time of sampling, which occurred during the operning of the domes and the making of the connections, whereas in the refinery in the Los Angeles area, the sampling was carried out, as a rule, after the connections had been made. The combined results, therefore, cover two stages of this operation. The exposure of the operator to the vapors during this entire period was negligible, because of his use of an effective (prescribed) respirator during this period. The results are

of interest and value, nevertheless, because of this demonstration of the order of magnitude of the potential exposure. The other operations associated with the movements of the concentrated antiknock compound in being mixed with gasoline, do not, as a rule result in a significant degree of contamination of the air within the mixing installation, inasmuch as they are carried out in a closed system under negative pressure. The analytical findings were in accord with expectations. It will be noted that the air outside the building which housed the mixing equipment in the San Francisco refinery contained more organic lead than did the inside. The reason for this was not ascertained, in view of fleeting character of the contamination of the air; it may well have been due to the position of the tank-cars or of the open vent, in relation to air currents, during the unloading of certain tank-cars.

The levels of concentration of organic lead in the air of the loading racks in the refinery in the Los Angeles area were higher than those in the other refinery (S.F.). The difference may have been due to the location of the sampling equipment in the two areas, or to climatic factors (See Appendix II and Appendix III). Here again, the combined results are more nearly indicative of the range of the potential exposure than either set of results alone.

The air was sampled during the filling of barrels with gasoline on but three occasions, with negligible results. The low frequency of the packaging of gasoline containing tetramethyllead, in this manner and under these conditions, justified the termination of these observations.

Thirty samples collected in the air of the technical laboratory yielded negative results. On one occasion out of four, a trace of organic lead was found in the inspection area on the wharf (known as the "long wharf").

2. At the Service Stations.

The total lead in the air of the service stations, Table 3, as sampled in San Francisco, averaged 0.28 micrograms per cubic foot (9.9 micrograms per cubic meter), of which 68 per cent. was organic and 32 per cent. inorganic. The corresponding results in Los Angeles, Table 4, were appreciably lower - total lead 0.13 microgram per cubic foot (4.6 micrograms per cubic meter), composed of 46 per cent. of organic, and 54 per cent. inorganic lead. The findings in Bakersfield, Table 5, with respect to total lead in the air at this one service station, differed somewhat in their distribution especially in the uppermost rubric (Table 5) i.e., the lower values, from those of both San Francisco and Los Angeles. The proportion of organic and inorganic lead in the total was also somewhat unlike either, lying just between them. These differences in the findings are slight, however, and are attributed more to differences in the manner of sampling than to significant differences in the environmental conditions. On the score of the prevalent ambient temperatures, one might have expected to find higher concentrations of organic lead in the air of service stations in Los Angeles than in San Francisco. The opposite relationship in the findings may be attributed to the fact that the actual point of sampling in Los Angeles was at the fueling islands but not in immediate proximity to the fueling procedure, while the technique

Table 3

Levels of Concentration of Lead in the Air at Ten Service Stations in San Francisco.

Ranges mic.g. per cu.ft.	Total Lead	Organic Lead	Inorganic Lead
0.0-0.09	115	169	185
0.1-0.19	31	-	56
0.2-0.29	32	39	11
0.3-0.39	24	1	9
0.4-0.49	4	-	3
0.5-0.59	26	38	1
0.6-0.69	12	2	-
0.7-0.79	3	1	1
0.8-0.89	3	-	-
0.9-0.99	0	-	-
1.0+	16	16	
Number	266	266	266
Mean	0.28	0.19	0.08
Std.Dev.	0.34	0.32	0.09
Median	0.16	0.08	0.07

Table 4

Levels of Concentration of Lead in the Air at Ten Service Stations in Los Angeles.

Ranges mic.g. per cu.ft.	Total Lead	Organic Lead	Inorganic Lead
0.0-0.09	192	258	250
0.1-0.19	59	29	48
0.2-0.29	29	17	11
0.3-0.39	16	7	2
0.4-0.49	11	1	6
0.5-0.59	6	4	1
0.6-0.69	2	-	2
0.7-0.79	1	-	1
0.8-0.89	-	-	-
0.9-0.99	-	-	-
1.0	5	3	-
Number	321	321	321
Mean	0.13	0.06	0.07
Std. Dev.	0.17	0.17	0.10
Median	0.085	0.06	0.065

Table 5

Levels of Concentration of Lead in the Air at One Service Station in Bakersfield

Ranges mic.g. per cu.ft.	Total Lead	Organic Lead	Inorganic Lead
0.0-0.09	11	25	13
0.1-0.19	7	2	12
0.2-0.299	4	2	2
0.3-0.39	3	-	1
0.4-0.49	2	-	2
0.5-0.59	1	-	1
0.6-0.69	1	-	1
0.7-0.79	-	-	-
0.8-0.89	-	-	-
0.9-0.99	-	-	-
1.0+	3	3	
Number	32	32	32
Mean	0.30	0.15	0.15
Std. Dev.	0.43	0.37	0.15
Median	0.19	0.065	0.125

in San Francisco involved locating the sampler about 2 feet lateral to the opening into the fuel tanks of automobiles and at the same level. This feature of the sampling had been left to the discretion of the persons who did the sampling, whereas it might properly have been agreed upon in advance. There is some advantage in having the two sets of data, whereby a fuller coverage of the potentialities for the exposure of personnel has been obtained. Moreover, it is important to recognize that the environmental conditions at the service stations are neither static nor uniform, so that the exposure is not only intermittent, but also varies with the location of the service station attendant in the performance of his various duties.

The data relative to organic lead in Tables 3 and 4 have been assembled in Tables 6 and 7 according to the volume of air sampled. It is evident that a large proportion of the individual findings fall within the range 0.0 to 0.09 micrograms of lead per cubic foot, regardless of the volume of the air sampled. Since the field method employed is incapable of the precise estimation of less than 0.5 microgram of lead per sample, lower results obtained by the analysis of the lead removed from a volume of 4 cubic feet mean only that the concentration of lead in the air was less than 0.125 microgram per cubic foot. Larger volumes of air were sampled, therefore, in an effort to obtain more precise results. It may be noted that the averages of the results obtained in the analysis of the lead from 8 and 12 cubic feet of air are in good agreement.

In the last column of Table 6 are listed data obtained by the

Table 6

The Frequencies of the Occurrence of the Ranges of Concentrations of Organic Lead in the Air of Service Stations in Los Angeles, as Distributed According to the Volume of Air Sampled.

Ranges mic.g. per cu.ft.	Field Method Cubic Feet of Air Sampled 4	8	12	16	20	Alternate Method 4 cu.ft. Crystalline Iodine
0 - 0.09	37	135	40	2	8	36
0.1 - 0.19		2	7		1	19
0.2 - 0.29		10	5			2
0.3 - 0.39		6				1
0.4 - 0.49						1
0.5 - 0.59		1	2			1
0.6 - 0.69						
0.7 - 0.79						
0.8 - 0.89						
0.9 - 0.99						
1.0+		5				
Number	37	159	54	2	9	60
Mean	0	0.07	0.06	0	0.01	0.08
Std. Dev.	0	0.10	0.12	0	0.03	0.10

Table 7

The Frequencies of the Occurrence of the Ranges of Concentration of Organic Lead in the Air of Service Stations in San Francisco, as Distributed, According to the Volume of Air Sampled.

Ranges mic.g. per cu.ft.	Cubic Feet of Air Sampled			
	4	8	12	16
0.0 - 0.09	77	70	10	12
0.1 - 0.19	-	-	-	-
0.2 - 0.29	-	23	1	15
0.3 - 0.39	-	-	1	-
0.4 - 0.49	-	-	-	-
0.5 - 0.59	2	14	7	15
0.6 - 0.69	-	-	1	1
0.7 - 0.79	-	1	-	-
0.8 - 0.89	-	-	-	-
0.9 - 0.99	-	-	-	-
1.0+	-	3	3	10
Number	79	111	23	53
Mean	0.02	0.20	0.32	0.44
Std. Dev.	0.11	0.29	0.40	0.44

use of a method of sampling, which, since these observations were made, has been published.* The crystalline iodine by which the vaporized organic lead was removed from the air, was sent to the Kettering Laboratory for analysis. As little as 0.1 microgram (0.025 microgram per cu.ft.) of total lead in the sample of 4 cu.ft. can be determined with prec sion by the analytical method ** employed. It is worthy of note that 29 of the 36 samples in this group failed to yield any lead, and that only 35 per cent. of the samples yielded concentrations in excess of 0.1 micrograms per cubic foot. These data offer additional evidence of the low order of the concentration of organic lead in the air of the service stations.

The data from the service stations in San Francisco (Table 7) agree with those in Table 6 in demonstrating that volumes of air greater than 4 cu.ft. were required for sampling, if precise results were to be obtained. Although the mean concentration of organic lead in the samples obtained in San Francisco (for a reason pointed out previously) was somewhat more than thrice that obtained in Los Angeles, the medium concentrations diverged but little (0.08 and 0.06 mic.g. per cu.ft. respectively, in San Francisco and Los Angeles).

In the Ambient Air of Central Areas in Los Angeles and San Francisco.

The data in Table 8 show that the average concentrations of particulate, inorganic lead in the air of Los Angeles (at the specific

* Snyder, L.J. and Henderson. S.R.: A new field method for the determination of organo-lead compounds in air. Anal. Chem. 33: 1175,1961.

**Cholak, J., Hubbard, D.M., and Burkey, R.E.: Micro determination of lead in biological materials. With dithizone extraction at high ph. Anal. Chem., 20: 671,1948.

Table 8

The Frequencies of Occurrence of the Levels of Concentration of Particulate Lead in Air, Within the Ranges Indicated, in Roughly Comparable Commercial Areas of Los Angeles and San Francisco

Ranges mic.g. per cu.m.	Los Angeles	San Francisco
0.0-0.99	3	21
1.0-1.99	23	49
2.0-2.99	45	24
3.0-3.99	37	13
4.0-4.99	19	5
5.0-5.99	15	-
6.0-6.99	18	-
7.0-7.99	1	-
8.0-8.99	4	1
9.0-9.99	1	-
10.0-10.99	1	-
11.0-11.99	4	-
12.0-12.99	1	-
13.0-13.99	0	-
14.0-14.99	1	-
15.0+	4	-
Number	177	113
Mean	4.3	1.8
Std. Dev.	3.14	1.44
Median	3.47	1.73

station) in San Francisco (1.8 mic.g. per cu.m.). These values may be compared with those of 5.2 and 2.4 mic.g. per cu.m. reported as having been found in Los Angeles and San Francisco, respectively, in 1954.* They are germane to the objectives of this investigation only to the extent that they relate to the general occurrence and the quantities of lead in the ambient atmosphere of urban areas. They are included here for what they may be worth as further contributions to the evidence indicative of the low order of magnitude of the concentration of lead in the air.

Another modest series of observations made incidentally, in the course of this investigation, as such observations have been made from time to time in the past, are assembled in Table 9. The extent of the contamination of the atmosphere with carbon monoxide in any area within which people work, move about or reside, is, obviously, worthy of investigation. The relationship of such observations to the exhausts of motor vehicles, in this instance, is self-evident, and the low order of the findings, as listed in Table 9, is significant in itself, as well as in its relationship to lead. The low concentration of carbon monoxide, derived from motor cars from which this gas is expelled in considerable volume and in fairly high concentration ($\pm$ 5 per cent. by volume in the exhaust), reveal in striking manner the rapidity and the extent of the dissipation of the products of combustion discharged from motor cars. Only 2 of 275 tests for carbon monoxide

* Chambers, L.A., Foter, M.J. and Cholak, J.: A Comparison of Particulate Loadings in the Atmospheres of Certain American Cities, Proc. 3rd Natnl. Air Poll. Symp. Pasadena, Cal. 1955; 24-32.

Table 9

The Frequencies of Occurrence of Certain Ranges of Concentration of Carbon Monoxide in the Air at Twenty Service Stations in Los Angeles and San Francisco

PPM Carbon Monoxide	Los Angeles	San Francisco
0 - 4.99	144	273
5 - 9.99	35	2
10 -15.99	6	
50 -54.99	1	
Number	186	275

made within the area of the service stations in San Francisco during the year were positive, and the two positive findings were at the lowest level of detection by the procedure employed, the sensitivity of which is of the order of 5 parts of carbon monoxide per million parts of air by volume. The proportion of positive findings in the service station in Los Angeles was considerably greater, the numbers being 42 of 186 tests. However, in all but 6 of these the levels of concentration were below 10 parts per million, the highest being 50 parts per million on a warm day on which the velocity of the wind was only 1 mile per hour.

Results of Observations on Men

1. Clinical Findings.

The initial examination of the men employed at the various sites constituted a repetition, in a somewhat more detailed manner, of the periodic examinations carried out on a schedule prescribed by the Medical Director of Standard Oil Company of California. As Indicated previously, a special set of record forms was designed for this purpose, and all of the information obtained - occupational and medical history, the results of a systematic physical examination, involving details of the status of the observed tissues, organs and organ systems, clinical urinalyses, hematological picture, and radiological findings - was forwarded to Cincinnati for clinical study, then for the coding of the findings and a systematic biometrical analysis. (The results of the serial analyses of the urine and blood for lead content were subjected likewise to statistical analysis, and will be dealt with separately, for reasons which will be made apparent.)

It was anticipated that a terminal round of examinations would be made by the same physicians in the same manner. This anticipation, however, was not realized, for the reason that by the end of the year of the investigation, the physicians, having been convinced by their early observation of the men, as well as by the results of the analyses of the urine and blood, that there was no justification for the repetition of the examinations in the initial manner, merely carried out such clinical procedures as were called for in dealing with employees scheduled for annual examinations (the men in the age groups above 40), and examined such others as appeared, for any reason, to be warranted. On this account, the data as recorded were unsatisfactory for biometrical comparison with those of the initial examination. Therefore, these data, in their entirety, are omitted from this report. The clinical information, therefore, may be summarized briefly, by saying that no man among the various groups of employees developed any illness, during the period of this investigation, which, by any stretching of clinical credulity, could have been suspected of being due to the absorption of any organic or inorganic compound of lead.

It should be said for the record that the failure to deal with the clinical portion of this investigation in a detailed statistical manner, while reducing the sharpness of the scientific procedure, subtracts nothing from the validity of the statement that none of these men sustained any definitive ill effects relative to the absorption of lead. The physicians who were responsible for the exercise of clinical critique as to the occupational safety of the employees, were somewhat

apprehensive during the early weeks of the introduction of tetramethyllead into gasoline, not having been completely convinced, by any previous evidence, that the actual day's work of the men would be free of hazard from the new gasoline . They were alert, therefore, for any complaint or sign of illness, and they requested that the results obtained by the analysis of the urine and blood in the first series and of the urine in subsequent series, be reported to them promptly. When no complaints came from the men, month by month, and as the analyses of the urine failed completely, as reported and interpreted, to yield any evidence of the absorption of lead by any of the men, the concern of the medical group relaxed into the routine of collecting samples at scheduled intervals, making casual observations as to the general health of the men, and being available for any further medical service that might be required.

The findings of the clinical laboratory, insofar as they relate to statistically significant variations in the hematological data, are worthy of additional presentation and comment. The data are presented in Table 10, where it will be noted that they show no change, curing the period of the investigation, which is even slightly suggestive of any deleterious effect, occupational or otherwise. There was indeed a change, an increase of statistically significant proportions, in the mean numbers of the erythrocytes in the blood of the group, when they were examined terminally, as compared with those found in the initial examination. The same was true of the hemoglobin content of the blood of these men. Whatever may be the

Table 10

The Numbers of Erythrocytes and the Amounts of Hemoglobin in the Peripheral Blood of Workmen at the Beginning and End of Sixteen Months of Employment in Occupations Involving Potential Exposure to the Vapor of Tetramethyllead

Time of Observations.	Numbers of persons observed.	Mean Numbers of Erythrocytes* in millions per cu. mm., and Standard Deviations	Mean Concentration o Hemoglobin* in gms. per 100 ml., and Standard Deviations
Initial	98	4.93 ± 0.35	14.38 ± 1.14
Terminal	44	5.30 ± 0.44	15.40 ± 1.08

* Includes all of the observations reported for the several groups of workmen.

explanation of the improvement in these qualities of the blood, which in the group, as well as in the large proportion of the individuals, occurred within wholly normal limits, it can hardly be construed to be the direct or indirect effect of the introduction of tetramethyllead into the gasoline handled by these men. It is pertinent here, again, to call attention to the fact that the absorption of tetramethyllead, as well as tetraethyllead, does not bring forth the hematological changes that often occur in response to the absorption of inorganic compounds of lead under appropriate conditions of dosage and time. The search by this means, therefore, for clinical evidence of the absorption of lead was, at once, a compliance with a clinical routine, the omission of which would have called forth criticism from certain quarters, and also a recognition of the fact that many of these men, notably the service station attendants, were being subjected to some degree of exposure to inorganic lead from the exhausts of automobiles. For what it may be worth as evidence, in this relationship, the findings have a negative significance.

2. The Analytical Findings.

The specific feature of the investigation, with respect to the degree of hazard of the absirption of lead incident to the use of tetramethyllead in gasoline, is that of the physiological signs of such absorption, or the lack of such signs, as represented in the analytical findings.

The data obtained by the analysis of the specimens of the urine of the individuals in the several groups of workmen are set forth in a systematic manner in Tables 11,12,13,14 and 15. Those

Table 11

The Urinary Excretion of Lead by Men Engaged in Mixing Antiknock Compound (Containing Tetramethyllead) with Gasoline.

Code Identification	Lead in Urine in Milligram per Liter: Initial Sample	Second	Third	Fourth	Fifth	All
B.I	0.03	0.015	0.015	0.015	0.015	0.018
B.2	0.045	0.015	0.02	0.025	0.015	0.020
B.3	0.015	0.015	0.015	0.020	0.015	0.016
B.4	0.03	0.015	0.025	0.015	0.040	0.025
B.5	0.03	0.025	0.015	0.015	0.030	0.023
Averages:	0.03	0.017	0.018	0.018	0.028	0.021

Table 12.

The Urinary Excretion of Lead by Men Engaged in Occupations Involving the Handling of Gasoline Containing Tetramethyllead.

Lead in Urine in Milligrams per Liter

Loaders of Tank Trucks

Code Identification	Initial Sample	Second	Third	Fourth	Fifth	All
L.1	0.018	0.015	-	0.015	0.015	0.016
L.2	0.03	0.015	-	0.035	0.015	0.024
L.3	0.015	0.11	0.03	0.015	0.025	0.039
L.4	0.02	0.03	0.02	0.020	0.015	0.021
L.5	0.015	0.015	0.015	0.030	0.020	0.019
L.6	0.035	0.07	0.03	0.040	0.030	0.039
L.7	0.055	0.055	0.05	0.050	0.030	0.048
L.8	0.032	0.06	0.025	0.045	-	0.041
L.9	0.045	-	-	-	-	-
L.10	0.02	0.02	0.015	0.020	0.015	0.018
L.11	0.015	0.02	0.015	0.010	0.015	0.015
L.12	0.030	0.015	0.035	0.020	-	0.02
L.13	0.015	0.015	0.015	0.015	0.015	0.015
Averages:	0.026	0.034	0.025	0.026	0.021	0.026

Table 13.

The Urinary Excretion of Lead by Men Engaged in Occupations Involving the Handling of Gasoline Containing Tetramethyllead.

Lead in Urine in Milligram per Liter

Barrel Fillers

Code Identification	Initial Sample	Second	Third	Fourth	Fifth	All
B.F.1	0.015	0.02	0.015	0.015	0.02	0.019
B.F.2	0.02	0.025	0.015	0.025	0.02	0.021
B.F.3	0.035	0.04	0.035	0.050	0.055	0.043
B.F.4	0.02	0.04	0.02	0.015	0.015	0.022
B.F.5	0.025	(0.12* (0.02	0.02	0.015	0.025	0.021
Averages:	0.025	0.029	0.021	0.024	0.027	0.025

Personnel of Laboratory

T.1	0.015	0.02	0.02	0.04	0.025	0.024
S.2	0.04	0.035	0.025	0.04	0.035	0.035
S.3	0.03	0.035	0.02	0.015	0.015	0.023
T.4	0.015	0.02	0.02	0.02	0.015	0.018
Averages:	0.025	0.027	0.021	0.029	0.023	0.025

Gaugers of Gasoline

G.L.1	0.03	0.015	0.015	0.025	0.020	0.021
G.2	0.05	0.015	0.02	0.025	0.015	0.025
G.3	0.015	0.02	0.025	0.015	0.015	0.018
G.4	0.02	0.015	0.015	0.025	0.015	0.018
G.5	0.05	0.015	0.02	0.030	0.015	0.024
Averages:	0.033	0.016	0.019	0.022	0.016	0.021

Wharf Inspectors

W.1.	0.01	0.03	0.02	-	0.015	0.019
W.2	0.025	0.02	0.015	-	0.020	0.020
W.3	0.03	0.045	0.025	0.065	0.020	0.037
W.4	0.015	0.055	-	0.015	0.015	0.025
Averages:	0.02	0.037	0.02	0.040	0.018	0.025

* Excluded in average.

Table 14

The Frequencies of Occurrence of Various Ranges of Concentration of Lead in the Urine of Service Station Attendants in the San Francisco Area, at Intervals of Approximately Three Months in Association with the Dispensing of Gasoline Containing Tetramethyllead

Lead in Urine Mg. per Liter	Initial Sample	Second	Third	Fourth	Fifth	All
0.01	6	3	11	-	12	32
0.02	8	10	8	6	8	40
0.03	7	4	2	6	1	20
0.04	3	5	2	3	2	15
0.05	1	2	-	5	1	9
0.06	1	1	1	-	-	3
0.07	1	-	-	-	-	1
0.06	-	1	1	-	-	2
0.15	1	-	-	-	-	1
Total Numbers	28	26	25	20	24	123
Mean	0.006	0.034	0.027	0.029	0.024	
St. Dev.	± 0.027	± 0.016	± 0.017	± 0.010	± 0.011	

Table 15

The Frequencies of Occurrence of Various Ranges of Concentration of Lead in the Urine of Service Station Attendants in the Los Angeles Area, at Intervals of Approximately Three Months, in Association with the Dispensing of Gasoline Containing Tetramethyllead

Lead in Urine Mg. per Liter	Initial Sample	Second	Third	Fourth	Fifth	All
0.01	5	11	7	11	3	37
0.02	8	11	10	9	7	45
0.03	9	4	9	7	5	34
0.04	8	1	2	1	4	16
0.05	2	1	-	-	-	3
0.06	2	-	-	-	-	2
0.20	1	-	-	-	-	1
Total Numbers	35	28	28	28	19	138
Mean	0.040	0.024	0.027	0.024	0.029	
St. Dev.	± 0.031	± 0.010	± 0.009	± 0.007	± 0.009	

concerned with the lead content of the blood of the same groups and individuals are given in Tables 16,17,18,19 and 20. In addition to the comparisons made possible by the manner of assembling the data in Tables 16 through 20, other comparisons of which Table 10 is illustrative, have been made by the statistical examination of all other serial observations that had been expressed in quantitative terms. The comparisons, in addition to those which appear in Table 10, concerned themselves with the volume and specific gravity of the specimens of urine of the entire group under investigation, as well as the separate groups which were sufficiently large for statistical purposes; they also involved various groupings of the data obtained by the analyses of the urine and blood, so as to seek out those which might be meaningful statistically. Although several statistically significant relationships were found, none of them go beyond the facts portrayed in Tables 16,17,18,19 and 20. That is, they bring out the same facts in somewhat greater detail, without throwing any further light upon their significance.

It may be noted that there was a slight but significant trend toward a decrease in the concentration of lead in the urine of most of the men in the various groups - especially significant is that of the service station attendants in both Los Angeles and San Francisco - and also in the concentration of lead in their blood, during the course of the investigation. No explanation is offered for this apparant trend, since one or more extraneous factors may have been responsible for it. In the course of investigations (approximate "balance" experiments) in which

Table 16

The Concentration of Lead in the Blood of Men Engaged in Mixing Antiknock Compound Containing Tetramethyllead with Gasoline

Lead in Blood in Milligram per 100 Grams

Code Identification	Initial Samples S	Initial Samples D	Terminal Samples S	Terminal Samples D	All
B.1.	0.03	0.02	0.02	0.015	0.021
B.2.	0.04	0.035	0.035	0.015	0.031
B.3.	0.025	0.025	0.02	0.015	0.021
B.4.	0.035	0.02	0.02	0.02	0.024
B.5.	0.02	0.02	0.02	0.025	0.021
Averages:	0.03	0.024	0.023	0.018	0.024

Table 17

The Concentration of Lead in the Blood of Men Engaged in Occupations Involving the Handling of Gasoline Containing Tetramethyllead

Lead in Blood in Milligram per 100 Grams

Loaders of Tank-trucks

Code Identification	Initial Samples		Terminal Samples		All
	S.	D.	S.	D.	
L.1	0.025	0.02	0.03	0.02	0.024
L.2	0.04	0.02	0.04	0.025	0.031
L.3	0.03	0.025	0.025	0.02	0.025
L.4	0.03	0.02	0.015	0.025	0.023
L.5	0.025	0.015	0.02	0.015	0.019
L.6	0.045	0.04	0.03	0.025	0.035
L.7	0.04	0.045	0.03	0.035	0.038
L.8	0.025	0.02	0.025	0.03	0.025
L.9	0.04	0.025	-	-	0.033
L.10	0.04	0.035	0.03	0.025	0.033
L.11	0.045	0.04	0.035	0.020	0.035
L.12	0.03	0.02	0.035	0.045	0.033
L.13	0.02	0.02	0.02	0.015	0.019
Averages:	0.033	0.027	0.028	0.025	0.029

Table 18

The Concentration of Lead in the Blood of Men Engaged in Occupations Involving the Handling of Gasoline Containing Tetramethyllead.

Lead in Blood in Milligram per 100 Grams

Barrel Fillers

Code Identification	Initial Samples S.	Initial Samples D.	Terminal Samples S.	Terminal Samples D.	All
B.F.1	0.035	0.03	0.03	0.02	0.029
B.F.2	0.025	0.025	0.025	0.02	0.024
B.F.3	0.025	0.03	0.03	0.03	0.029
B.F.4	0.025	0.02	0.025	0.015	0.023
B.F.5	0.025	0.02	0.020	0.015	0.020
Averages:	0.027	0.025	0.026	0.020	0.025

Personnel of Laboratory

T.1.	0.02	0.015	0.025	0.025	0.021
S.2	0.04	0.025	0.035	0.025	0.031
S.3	0.02	0.02	0.02	0.02	0.02
T.4	0.02	0.02	0.03	0.02	0.025
Averages:	0.025	0.02	0.028	0.023	0.024

Gaugers of Gasoline

G.L.1	0.04	0.02	0.02	0.02	0.025
G. 2	0.04	0.02	0.025	0.025	0.028
G. 3	0.02	0.015	0.025	0.02	0.02
G. 4	0.04	0.02	0.035	0.015	0.028
G. 5	0.03	0.02	0.045	0.02	0.029
Averages:	0.034	0.019	0.030	0.02	0.026

Wharf Inspectors

W.1	0.015	0.02	0.03	0.025	0.023
W.2	0.03	0.025	0.02	0.02	0.024
W.3	0.05	0.03	0.035	0.035	0.038
W.4	0.02	0.02	0.03	0.02	0.023
Averages:	0.029	0.024	0.029	0.025	0.027

Table 19

The Frequencies of Occurrence of Various Ranges of Concentration of Lead in the Blood of Service Station Attendants in the San Francisco Area, at an Interval of Approximately 15 Months in Association with the Dispensing of Gasoline Containing Tetramethyllead

Lead in Blood Mg. per 100 Grams	Initial Samples S.	Initial Samples D.	Terminal Samples S.	Terminal Samples D.	All
0.01				1	1
0.02	6	16	11	17	52
0.03	11	8	9	5	33
0.04	6	3	3	1	13
0.05	3	-	1	-	4
Total Numbers.	28	27	24	24	103
Mean.	0.036	0.029	0.031	0.026	
St. Dev.	± 0.009	± 0.007	± 0.008	± 0.005	

Table 20

The Frequencies of Occurrence of Various Ranges of Concentration of Lead in the Blood of Service Station Attendants in the Los Angeles Area, at an Interval of Approximately 15 Months, in Association with the Dispensing of Gasoline Containing Tetramethyllead.

Lead in Blood Mg. per 100 Grams.	Initial Samples		Terminal Samples		All
	S	D	S	D	
0.01	1	2		2	5
0.02	7	16	5	11	39
0.03	11	9	10	5	35
0.04	9	3	3	1	16
0.05	2	2	-	-	4
0.06	-	1	-	-	1
0.07	1*	1*	-	-	2
0.08	2*	1*	-	-	3
Total Numbers:	33	35	18	19	105
Mean.	0.040	0.035	0.033	0.027	
St. Dev.	± 0.015	± 0.016	± 0.007	± 0.006	

* Sampling repeated - low normal results obtained.

experimental subjects have been collecting duplicates of everything eaten and drunk, as well as all urine and feces, day by day, over prolonged periods of time, it has been observed that the rate of the urinary excretion of lead, as well as the concentration of lead in the blood, rise and fall slightly, from time to time, with a variety of factors which affect principally the quality and quantity of the food and beverages consumed. It seems unlikely that factors of this type operate in the same direction within large populations, but they may do so in a fairly homogeneous and small group, and moreover, there are seasonal influences that exert their effects. In any case, it is clear that these men sustained no significant increase in their occupational exposure to, and absorption of, lead. Here again, as in the variability of the findings in the blood, it is impossible to interpret the significance of minor changes within normal limits unless all of the influential factors are being controlled.

Certain comments should be made concerning specific items of data that are listed in the tables of this section of the report. Attention may be called, first, to the fact that certain samples of urine were too small in volume to be entirely acceptable on physiological grounds, as being even approximately representative of the rate of excretion of lead over any considerable period of time. Almost every result obtained by the analysis of such samples turned out to be well within the usual "normal" range, and so they were included within the group of results. When the concentration of lead in the blood of a man whose specimen of urine had been somewhat less than satisfactory, was found to be well within the usual "normal" range, and so they were included within

the group of results. When the concentration of lead in the blood of a man whose specimen of urine had been somewhat less than satisfactory, was found to be well within the "normal" range (as was generally the case), there was no valid reason for doubting the essential validity of the normal result obtained by the analysis of his urine, regardless of its volume.

As a further point to be considered, not all samples of blood were obtained in duplicate (as indicated previously), and when this was the case, the single sample was analysed by the two methods. Under these circumstances no check as to the possible contamination of the sample was provided. The importance of this omission is illustrated by certain of the high results in Table 20 which are singled out by asterisks. In one instance of this type, both analytical results were in excess of 0.08 mg. per 100 grams of blood. On reporting these results, to the responsible physician the prompt collection of additional duplicate samples was requested, since, if the initial results were correct, this employee had absorbed a dangerously large quantity of lead from some source. The duplicate samples were obtained and analysed, yielding (by the two methods) 0.020 and 0.025 mg. of lead per 100 grams of blood. Obviously, the initial sample had been contaminated in some manner. In two other instances, a single sample of blood of inadequate size was obtained, one of 2 grams, the other of 4.4 f.f grams. The analytical error in such instances is augmented by the minuteness of the quantity of lead available for analysis, and is further multiplied in the calculation of the result for conventional expression. The sample of 2 grams yielded the calculated value of 0.07 mg. of lead per 100 grams; when a subsequent

pair of satisfactory samples was analysed, the average result was 0.03 mg. per 100 grams. The sample which weighed 4.4. grams, when analysed by the two methods, yielded 0.08 and 0.05 mg. of lead per 100 grams. Subsequent duplicate samples gave the average value of 0.02 mg. per 100 grams. The one other pair of high results recorded in Table 20 was obtained by dual analyses of a single sample of smaller size than is desirable, weighing 7.1 grams; the parallel analyses yielded 0.07 and 0.06 mg. per 100 grams, which while not in the dangerous range of values, is clearly indicative, if valid, of an unusual degree of absorption of lead. The facts in this instance were not determined by further analyses or by any other means, since this man was unwilling to coöperate further in the investigation. (It is not the best practice, in investigations of this type, to accept for analysis any but wholly satisfactory samples, since every aberrant finding requires further investigation, which is not always feasible. The recitation of the foregoing details illustrates this point, and also calls attention to some of the difficulties that arise in the conduct of an investigation at considerable distance.)

A few individual results obtained by the analysis of specimens of urine also deviated appreciably from the general statistical universe represented by the data as a whole. These results, four in all, are in no wise remarkable, since samples of urine collected with the most minute care are contaminated with lead from time to time. They have been included in the tables, and they have also been examined

individually in their specific relationships. The facts concerning them are as follows:-

In Table 12, under "Loaders of Tank-trucks", a result in the second column, of 0.11 mg. per liter (which is near but not beyond the upper normal limit of the concentration of lead in a sample of urine of small volume) is obviously abberrant in the statistical sense and is probably invalid, because of the results obtained by the analysis of the first and third samples of this same person, 0.015 and 0.03 mg. respectively, per liter. (The value of 0.07mg. per liter which occurs in the same column of this table is not to be taken too seriously, from the aspect of any physiological meaning which it might have otherwise, because of its small volume, by which the analytical error may have been magnified. It is not, of course , remarkably high, but it stands out by comparison with the other values in this table.)

In Table 13, under "Barrel Fillers", is a result of 0.12 mg. per liter. This was sufficiently unusual, especially in this small group of men engaged in an occupation that might (under certain unusual circumstances) give rise to a significant degree of exposure, that a further sample was called for and obtained; on analysis it yielded the value of 0.02 mg. per liter. The prior and subsequent samples voided by this man may be seen to have been 0.025 and 0.02 mg. respectively, per liter. This relatively high finding can be dismissed from further consideration.

In Table 14, is a single result, obtained in the first round of observations, of 0.15 mg. per liter. This finding in the urine of a service station attendant could not be regarded as evidence of a dangerous occupational condition, and its aberrant character could

be inferred from its unique relationship to the many others in the same category. Accordingly it was not checked by obtaining a further sample at once. The results obtained in the second and third samples from this same subject were 0.025 and 0.045 mg. respectively, per liter.

Essentially the same situation as that above is repeated in Table 15, in which a result of 0.20 mg. per liter, obtained on the first round of sampling, was followed by the finding of 0.015 and 0.02 mg. respectively, per liter, in the second and third samples from the same man.

An additional comment may serve a useful purpose in relation to the urinary findings. The idea has been advanced and has gained credence in certain circles, that samples of urine of small volume, such as those voided at one time, do not convey valid information concerning the general level of the urinary excretion of lead. This is true only of individual samples that are of small volume because of the unavailability of suitable quantities of water within the body of the person who supplies the sample, or of samples of unusually large volume voided at a time when the throughput of water is unusually high. (This statement is predicated, of course on the assumption that the renal function is essentially normal.) In short, a highly concentrated sample of urine will contain an unusually high concentration of lead, while a highly dilute sample will yield the opposite result. Attempts have been made to "correct" the analytical result to a standard specific gravity, or a standard concentration of some allegedly invariable or less variable constituent

of the urine. Thus far, no such correction factor can be held to be valid, even though it may move the aberrant result somewhat closer to the mean or medium value of a related group of results. The correction is especially questionable in dealing with the extremes of concentration, and it cannot be counted on to do more than artificially to reduce the variability of a series of results. This artificial and often misleading procedure has not been considered for application to the results presented herein. Rather, we have relied upon a broad experience with a wide variety of results obtained by methods comparable to those employed in this instance, which, without artifice, have supplied the background for the differentiation of "normal" from "abnormal" results. Finally, it should be said that the comparison of a series of samples of urine of small volume with samples of large volume from the same individuals, shows the former to be somewhat more widely variable at both ends of the spectrum, i.e., the small samples made a wider universe, but there is little difference, otherwise, in the distribution and the statistical characteristics of the two sets of results. For the purposes of this investigation, the lower incidence of the contamination of small samples, collected under instruction and supervision greatly outweighed the advantage which might otherwise have been gained from samples of large volume, while the vagaries of variability, in the case of individual samples, are blotted out by resort to multiple samples from the same individual and by numbers of individual samples obtained from reasonably homogeneous groups of persons.

strictly normal variability) in the concentration of lead in the urine of an individual member of these small groups.

The statistical comparison of the levels of lead concentration in the urine of the two larger groups of service station attendants in San Francisco and Los Angeles revealed certain inconsistent differences. These differences, while of statistically significant magnitude in some instances, cannot be regarded as of physiological significance in relation to the hygienic question under investigation, because of their erratic occurrence in time. Moreover, all of the differences noted are within the range of normal or incidental variability and, therefore, must be accepted as being within the range of the deviations associated with the general methods of investigation.

The statistical comparison of the data obtained at the five serial stages of the investigation from each of the two groups of filling station attendants also reveals certain differences within the individual groups. These differences have the same characteristics as those referred to above, and, therefore, are of no significance in relation to the primary problem of this investigation.

APPENDIX

APPENDIX I

Method for the Determination of Lead in Material Collected on Millipore Filters Type AA. 57 mm. in Diameter

Solutions

1. Conditioned chloroform - Place 1 liter of reagent chloroform, or chloroform redistilled from a borosilicate glass still, in a 2 liter, glass-stoppered, borosilicate glass separatory funnel. Dissolve approximately 10 grams of hydroxylamine hydrochloride in 50 ml. of distilled water and make the solution alkaline to phenol red indicator by the addition of reagent grade ammonium hydroxide. Add this solution to the chloroform in the separatory funnel and shake well. Allow the aqueous layer to separate and filter the chloroform through a fluted filter paper into a brown, glass-stoppered bottle containing 20 ml. of absolute alcohol. Shake well and store in a refrigerator.

2. Dithizone Solutions

(a) Stock solution - 40 mg. of dithizone per liter of conditioned chloroform (store in a brown bottle in a refrigerator).

(b) Working solution - 50 milliliters of solution (a) diluted to 200 ml. with conditioned chloroform. This solution is prepared daily.

3. Buffer Solution - Place 500 grams of citric acid in a beaker, add 350 ml. of double-distilled water and a few (6) drops of (U.S.P.) phenol red indicator. Add reagent grade ammonium hydroxide slowly until the solution is alkaline (pink). Cool and add 25 grams

of potassium cyanide, 25 grams of hydroxylamine hydrochloride, and dilute with double-distilled water to 1250 milliliters. De-lead this solution by shaking it repeatedly with 10 ml. portions of dithizone stock solution (a) until the dithizone retains its original green color. When the solution has been de-leaded, remove the excess of dithizone by extracting repeatedly with small portions of chloroform. Add 2500 ml. of reagent ammonium hydroxide. Store in a refrigerator.

METHOD

1. Preparation of samples

   (a) Place the filter in a 100 ml. pyrex beaker de-leaded by rinsing it with 50% nitric acid. Add:

   5 ml. of double-distilled water

   5 ml. of concentrated nitric acid (C.P. Reagent)

   3 ml. of concentrated sulfuric acid (C.P. Reagent)

   0.5 ml. of 70% perchloric acid (Mallinckrodt A.P.)

   Digest on a hot plate. If charring occurs treat with 1 ml. portions of nitric acid. Finally heat just to fumes of sulfur trioxide. Cool, and rinse the sample into a 125 ml. graduated separatory funnel with a minimum of double-distilled water (20 cc).

2. Add 2 drops of phenol red indicator.

3. Add reagent grade ammonium hydroxide until the sample is alkaline (red).

4. Using the graduation marks on the 125 ml. extraction funnel, make the sample up to 40 ml. with double-distilled water.

5. Add accurately 15 ml. of working dithizone solution (b). Then add 30 ml. of the buffer solution and mix well.
6. Shake for one minute.
7. Run the dithizone solution through a pledget of cotton into a 50 mm. cell after discarding the first 2 ml. of solution.
8. Determine the absorption with a photometer at wave length 510 mu. The instrument is set to zero with conditioned chloroform and all readings are made against conditioned chloroform. A clean Millipore filter is carried through the entire procedure in order to set the zero of the calibration graph derived according to the procedures outlined in step 9. A new graph from which the concentration of lead is obtained is drawn parallel to the original graph but passing through the new zero.
9. The original calibration graph is prepared by adding known amounts of lead (0-14) to circles of Millipore filters and carrying the procedure through exactly as the samples.

Notes:

The single extraction procedure should be used only with strict standardization and control of the size of sample and the quantities of reagents. Each change in the type or size of the filter medium or in the quantities of reagents necessitates the derivation of a separate calibration graph, good only for the changed conditions.

APPENDIX II

Comparison of the Frequencies of Occurrence of Certain Ranges of Temperature (°F) in Los Angeles and San Francisco

Range of Temperature in Degrees Fahrenheit	Los Angeles	San Francisco
30 - 34.9		3
35 - 39.9		7
40 - 44.9	5	12
45 - 49.9	2	19
50 - 54.9	6	12
55 - 59.9	16	32
60 - 64.9	44	92
65 - 69.9	196	152
70 - 74.9	172	125
75 - 79.9	118	45
80 - 84.9	118	22
85 - 89.9	68	4
90 - 94.9	70	
95 - 99.9	40	
100	12	
Number	867	525
Mean	76.8°F	66.6°F
Std. Dev.	10.8	9.15
Median	75.4	67.8

APPENDIX III

The Frequencies of Occurrence of Certain Ranges of the Velocity of Wind in Los Angeles and San Francisco

Range of Velocity of Wind in Miles/Hr.	Los Angeles	San Francisco
0 - 4.9	599	183
5 - 9.9	207	190
10 -14.9	25	94
15 -19.9	4	38
20 -24.9	2	12
25 -29.9		6
30 -34.9		1
Number	873	524
Mean Velocity	4.1 mph	8.0 mph
Std. Dev.	2.9	5.6
Median	3.5	6.9