Comments Concerning,

AIR QUALITY CRITERIA FOR LEAD

Second Draft

CHAPTER I

INTRODUCTION

Line 2 of the Introduction contains the word "lethal" to characterize the toxic properties of lead, presumably for man. Since the "lethal" effect is indeed rare, in relation to air-borne lead, except in the case of herbivorous animals, whose forage has been contaminated seriously by the "fall-out" of lead emitted from near by smelters, especially secondary smelters, or other industrial establishments in which lead is melted, refined or alloyed*, this is an unfortunate, if simply ill chosen, expression. It might be suspected that, for reasons other than lack of experience or knowledge, the choice was made of an expression which would convey the direst possible connotations of the anticipated effect of the absorption of lead from the ambient atmosphere. This matter of verbage, is not, of itself, important, except, perhaps, as an indication of an attitude toward the subject, which should be dealt with in the most soberly critical manner, rather than to make use of histrionics, in view of the available and relevant information.

Moreover, the next to last paragraph of the introduction provides little comfort to those who would look to this document for a sound presentation of the facts as to the significance of the information now available concerning the actually and potentially harmful effects of the current contamination of the ambient air with lead. The process of the "distillation of information" from the observations and publications

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* The serious problem of lead poisoning in infancy and childhood, when, because of the innocent or abnormal behavior of that period, large quantities of lead (usually in the form of paint) may be ingested (swallowed), with lethal effects all too often, is not related to air-borne lead.

Table 13

Distribution of Workmen Employed on Mixing Tetraethyl lead with Gasoline according to Milligrams of Lead per Liter of Urine

Milligrams of Lead per Liter of Urine	1927		1929		1931		Combined	
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percentage
0-0.01	2	5.6	2	5.0	19	41.3	23	18
0.02-0.03	4	11.1	10	25.0	14	30.4	28	23
0.04-0.05	11	30.5	8	20.0	6	13.0	25	20
0.06-0.07	9	25.0	8	20.0	2	4.3	19	15
0.08-0.09	4	11.1	6	15.0	1	2.2	11	9
0.10-0.11	3	8.3	2	5.0			5	4
0.12-0.13	2	5.6	2	5.0			4	3
0.14-0.15			1	2.5	1	2.2	2	2
0.16-0.17			1	2.5	1	2.2	2	2
0.18-0.19	1	2.8					1	1
0.20-					2*	4.3	2*	2
Total	36	100.0	40	100.0	46	100.0	122	100
Mean	0.068		0.066		0.033		0.055	
Probable Error of Mean	± 0.004		± 0.004		± 0.003		± 0.002	
Standard Deviation	± 0.036		± 0.037		± 0.034		± 0.039	

* Two results 0.32 and 0.64 excluded in calculation of means

KE 01399

Table 12

Distribution of Workmen Employed in Mixing Tetraethyl Lead with Gasoline According to Milligrams of Lead per Liter of Urine

Milligrams of Lead Per Liter of Urine	1927		1929		1931		Composite	
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percen
0-0.01	2	5.6	2	5.0	19	41.3	23	18.
0.02-0.03	4	11.1	10	25.0	14	30.4	28	23.
0.04-0.05	11	30.5	8	20.0	6	13.0	25	20.
0.06-0.07	9	25.0	8	20.0	2	4.3	19	15.
0.08-0.09	4	11.1	6	15.0	1	2.2	11	9.
0.10-0.11	3	8.3	2	5.0			5	4.
0.12-0.13	2	5.6	2	5.0			4	3.
0.14-0.15			1	2.5	1	2.2	2	1.6
0.16-0.17			1	2.5	1	2.2	2	1.6
0.18-0.19	1	2.8					1	0.8
0.20-					2*	4.3	2*	1.6
Totals	36	100.0	40	100.0	46	100.0	122	100.

Mean	0.068	0.066	0.033	0.055
Probable Error of Mean	± 0.004	± 0.004	± 0.003	± 0.002
Standard Deviation	± 0.036	± 0.037	± 0.034	± 0.039

* Two results 0.32 and 0.64 excluded in calculation of means.

KE 01400

Table 12

Distribution of Workmen Employed in Mixing Tetraethyl Lead with Gasoline According to Milligrams of Lead per Liter of Urine

Milligrams of Lead Per Liter of Urine	1927		1929		1931		Composite	
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percen
0-0.01	2	5.6	2	5.0	19	41.3	23	18.9
0.02-0.03	4	11.1	10	25.0	14	30.4	28	23.(
0.04-0.05	11	30.5	8	20.0	6	13.0	25	20.5
0.06-0.07	9	25.0	8	20.0	2	4.3	19	15.6
0.08-0.09	4	11.1	6	15.0	1	2.2	11	9.(
0.10-0.11	3	8.3	2	5.0			5	4.1
0.12-0.13	2	5.6	2	5.0			4	3.3
0.14-0.15			1	2.5	1	2.2	2	1.6
0.16-0.17			1	2.5	1	2.2	2	1.6
0.18-0.19	1	2.8					1	0.8
0.20-					2*	4.3	2*	1.6
Totals	36	100.0	40	100.0	46	100.0	122	100.(

Mean	0.068	0.066	0.033	0.055
Probable Error of Mean	± 0.004	± 0.004	± 0.003	± 0.002
Standard Deviation	± 0.036	± 0.037	± 0.034	± 0.039

* Two results 0.32 and 0.64 excluded in calculation of means.

KE 01401

Table 12

Distribution of Workmen Employed in Mixing Tetraethyl Lead with Gasoline According to Milligrams of Lead per Liter of Urine

Milligrams of Lead Per Liter of Urine	1927		1929		1931		Composite	
	Number	Percentage	Number	Percentage	Number	Percentage	Number	Percen
0-0.01	2	5.6	2	5.0	19	41.3	23	18.
0.02-0.03	4	11.1	10	25.0	14	30.4	28	23.
0.04-0.05	11	30.5	8	20.0	6	13.0	25	20.
0.06-0.07	9	25.0	8	20.0	2	4.3	19	15.
0.08-0.09	4	11.1	6	15.0	1	2.2	11	9.
0.10-0.11	3	8.3	2	5.0			5	4.
0.12-0.13	2	5.6	2	5.0			4	3.
0.14-0.15			1	2.5	1	2.2	2	1.
0.16-0.17			1	2.5	1	2.2	2	1.
0.18-0.19	1	2.8					1	0.
0.20-					2*	4.3	2*	1.6
Totals	36	100.0	40	100.0	46	100.0	122	100.

Mean	0.068	0.066	0.033	0.055
Probable error of mean	± 0.004	± 0.004	± 0.003	± 0.002
Standard Deviation	± 0.036	± 0.037	± 0.034	± 0.039

* Two results 0.32 and 0.64 excluded in calculation of means.

ICE 01402

Table

Distribution of [illegible] Timothy [illegible]
Seeded to Different Lengths

Stubble [illegible]	1927		1928		1931		[illegible]
50 Heads							
0	25	69.6	17	43.5	16	34.8	[illegible]
1-4	10	27.0	8	20.5	13	28.2	[illegible]
5-8	2	5.4	1	2.6	7	15.2	[illegible]
9-12			4	10.2	5	10.9	[illegible]
13-16			3	7.7			[illegible]
17-20			1	2.6	1	2.2	[illegible]
21-24			1	2.6	1	2.2	[illegible]
25-49			1	2.6	3	6.5	[illegible]
50-74			3	7.7			[illegible]
Total	37	100.0	39	100.0	46	100.0	122

Approximate Mean Inches available

[illegible]

Should be calculated mean.

01403

Approximate Mean	1.66 ⊕	5.06	4.40	3.79
Probable Error of Mean	± 0.22	± 0.67	± 0.54	± 0.31
Standard Deviation	± 2.02	± 5.88	± 5.22	± 4.85

⊕ Calculated on a wider distribution

Table

Summary of Mean Values of lead found in Single Samples of Faeces, of Lead in Milligrams per [illegible] of Lead in Milligrams per Litre of Urine, and of Stippling of Erythrocytes, for Various Groups of Workers employed and not employed in the Lead Trades.

[illegible]	Workers in White Lead Plant	Workers in Red Lead and Litharge Manufacturing Plant	Workers in Tetraethyl Lead Manufacturing Plant	Workers Employed in Mixing Tetraethyl Lead in Motor Fuel	Persons employed outside the Lead Trades
Lead in Milligrams in Total Single Sample of Faeces	3.76 ± 0.24	2.53 ± 0.18	0.42 ± 0.01	0.26 ± 0.01	0.20 ± 0.01
Lead in Milligrams per Litre of Lead in Faeces	0.57 ± 0.03	0.45 ± 0.03	0.19 ± 0.01	0.07 ± 0.01	0.07 ± 0.01
Lead in Milligrams per Litre of Urine	0.24 ± 0.01	0.18 ± 0.01	0.13 ± 0.01	0.06 ± 0.01	0.07 ± 0.01
Number of Subjects in Observations	86	71	170	122	167
Significance of Lead Effects	Associated with Occurrence of Plumbism	Associated with Occurrence of Plumbism	No occurrence of Plumbism in 5 years	No occurrence of Plumbism	No occurrence of Plumbism
Stippling of Erythrocytes in 50 fields	18.73 ± 1.66	9.79 ± 1.48	10.77 ± 0.68	8.79 ± 0.31	1.4 ± 0.2

[illegible] 01404

Insert [illegible]

4. The lead Excretion of Workers Employed in Mixing Tetraethyl Lead with Gasoline

Tetraethyl Lead (Compounded with various other materials) is mixed with gasoline at gasoline refineries and large gasoline storage houses. From one to three men are required at each of such points to carry out all the functions which require any handling of the lead compound or its containers. The actual mixing is accomplished by means of special equipment, and the precautionary measures surrounding the operation are such that the absorption of lead may be avoided entirely. Moreover, there is no opportunity for daily exposure, since mixing is not done more frequently than once a week except in unusual circumstances. The potential hazards in the handling of such a material as tetraethyl lead are very great. However, under the conditions which prevail at these mixing plants, the practical hazards are so limited that few new cases of lead poisoning and fatality never except by reason of carelessness on the part of the personal, or as the result of some unusual accident. The lead exposure of this group of workmen is known to be negligible, under present conditions. Nevertheless, considering the necessity for the maintenance of the precautionary measures, they are kept under medical supervision, and from time to time a representative group of the workmen is selected for a study of their lead excretion. The results of all such observations are presented in tabular form in order to illustrate, further, the relationship between the excretion of lead and the degree of lead exposure.

Tables —, —, and — give the analytical findings on the faeces and urine; while —, shows the results of the microscopic examinations of the blood. The comparison of these with the corresponding results obtained among lead workers and the normal population show that they

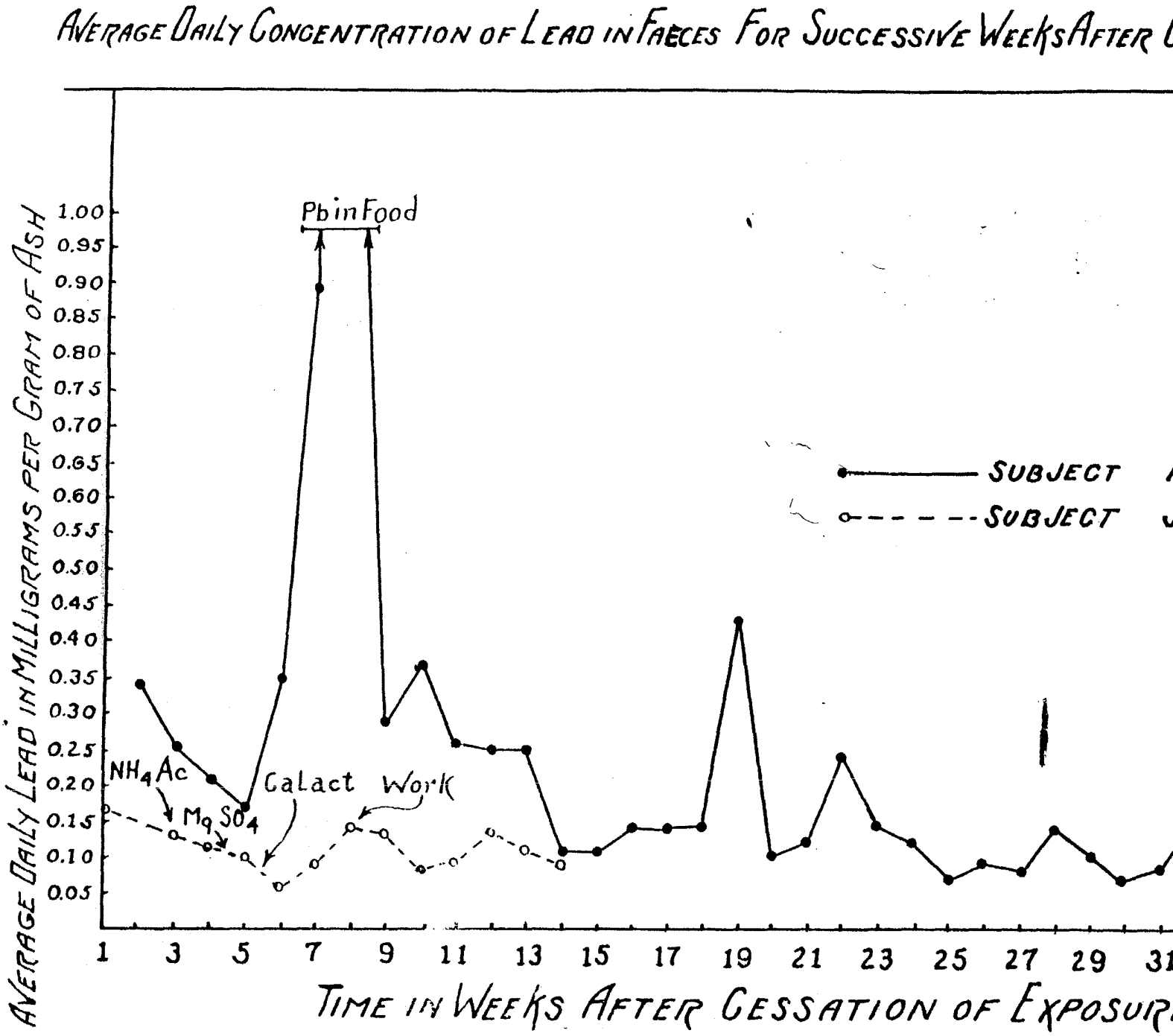
facilitating their comparison. Table — gives the arithmetic values of the temperature of the subjects. The

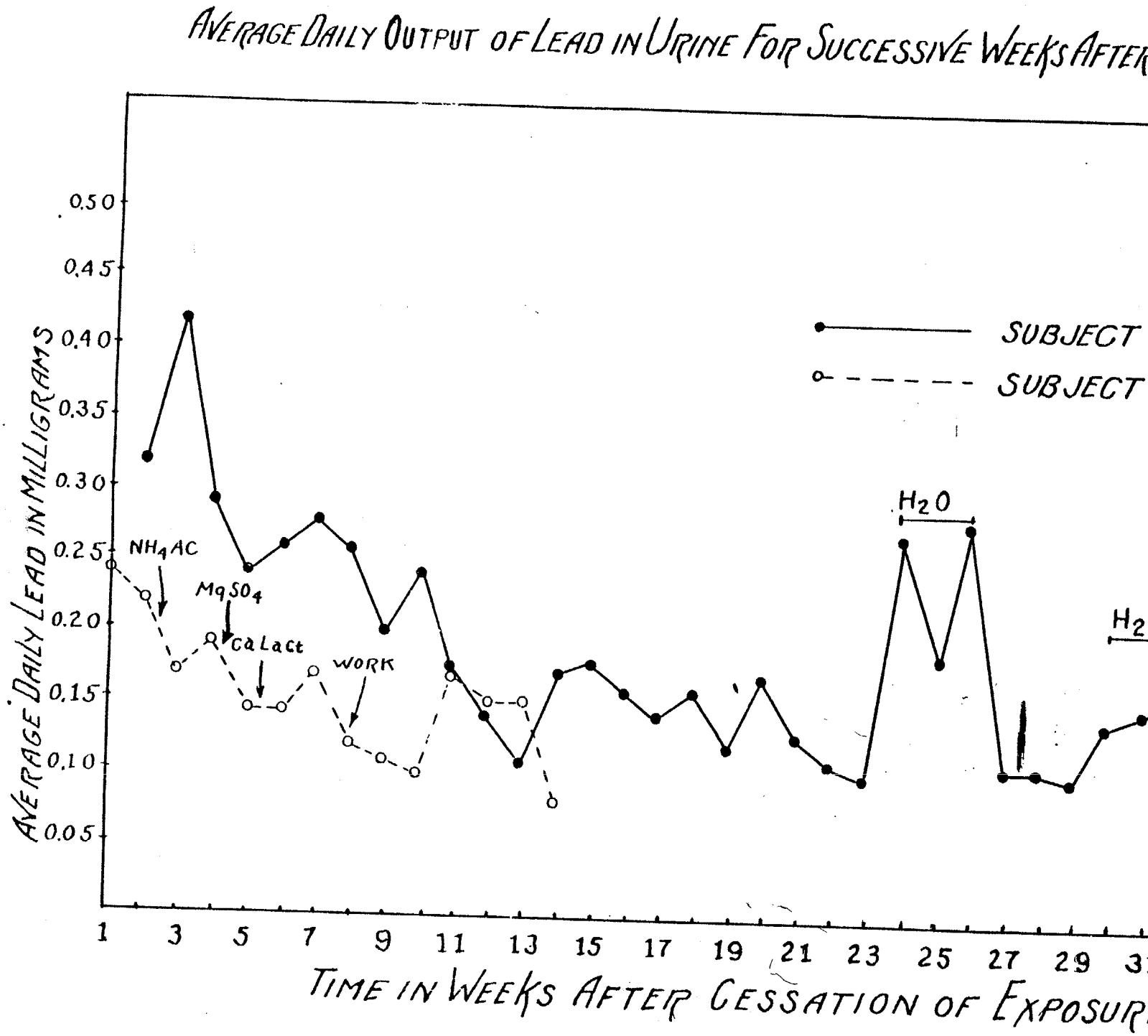
5. Lead Excretion After the Cessation of Occupational Lead Exposure.

The foregoing observations have demonstrated that the ~~rate of~~ lead excretion of groups of individuals varies with the extent of their exposure to lead compounds. It would be difficult to overemphasize the importance of this fact in its practical application to the measurement of lead exposure in the various lead trades. However the information furnished thus far does not give any indication of the extent of lead absorption into the tissues, under conditions of industrial exposure. Such absorption must occur, and it must be accumulative to a degree, in order to produce intoxication. The extent of the absorption and accumulation is therefore a matter of prime importance. Such knowledge, ~~as~~ applicable to the ~~determination~~ industrial worker is to be obtained only by indirect methods. We may further by inquire, therefore, as to what extent the excretion of lead is dependent upon the quantity of lead absorbed by the tissues. An attempt to obtain some knowledge of this type resulted in the observations which are detailed in Figure —.

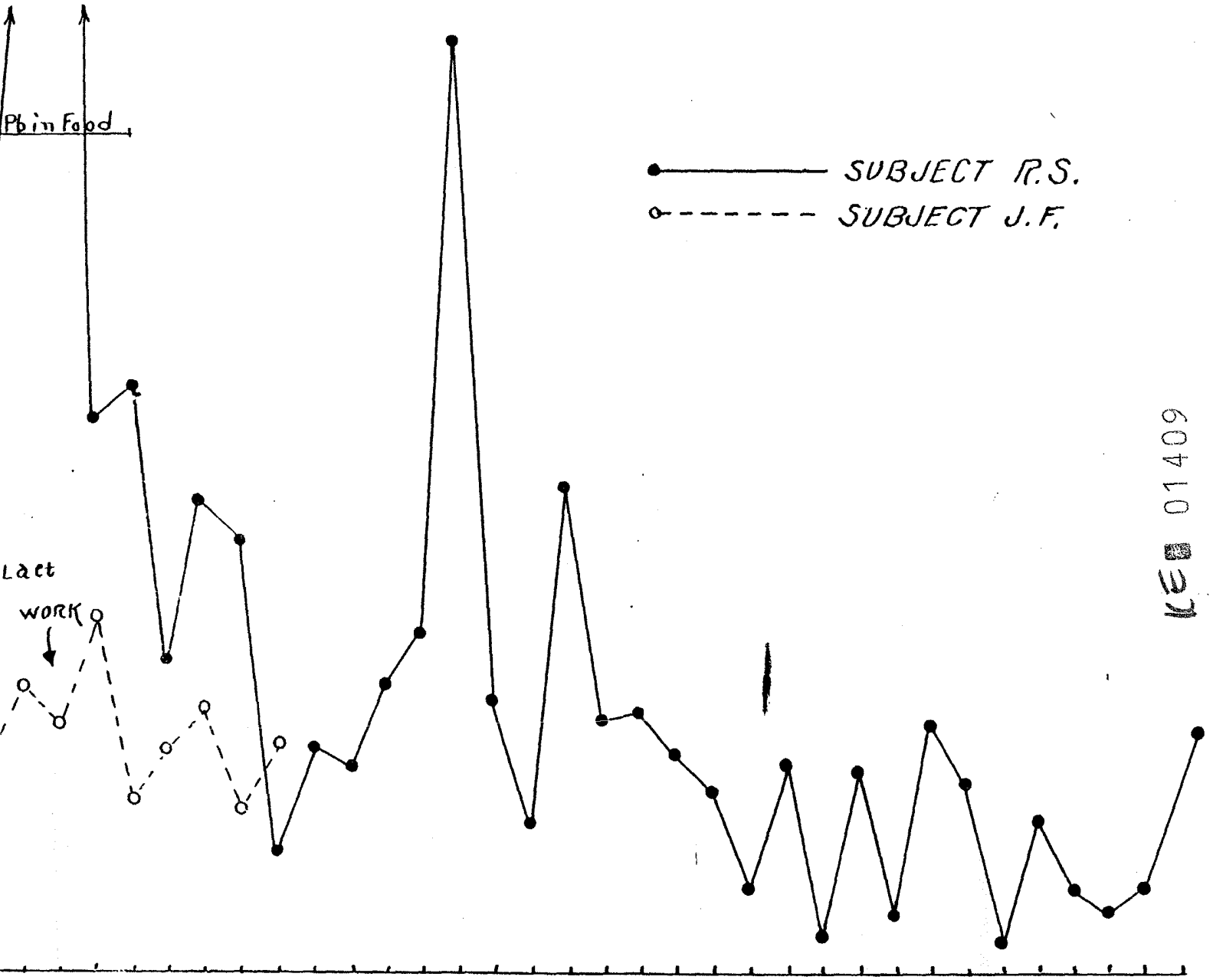
LE 01406

The subject of these observations, a negro of ~~of~~ age, came to our attention as the result of an episode of lead intoxication. He had been occupied intermittently over a period of 7 years in various white lead plants. His last exposure was of a severe type. ~~a~~ After ~~[illegible]~~ he had developed colic and was compelled to relinquish his work. He was seen at the laboratory ~~three weeks~~ afterward, at which time the observations recorded in


AVERAGE DAILY CONCENTRATION OF LEAD IN FAECES FOR SUCCESSIVE WEEKS AFTER
AVERAGE DAILY LEAD IN MILLIGRAMS PER GRAM OF ASH
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
Pb in Food
NH4Ac
MgSO4
Galact
Work
SUBJECT
SUBJECT
1
3
5
7
9
11
13
15
17
19
21
23
25
27
29
31
TIME IN WEEKS AFTER CESSATION OF EXPOSUR

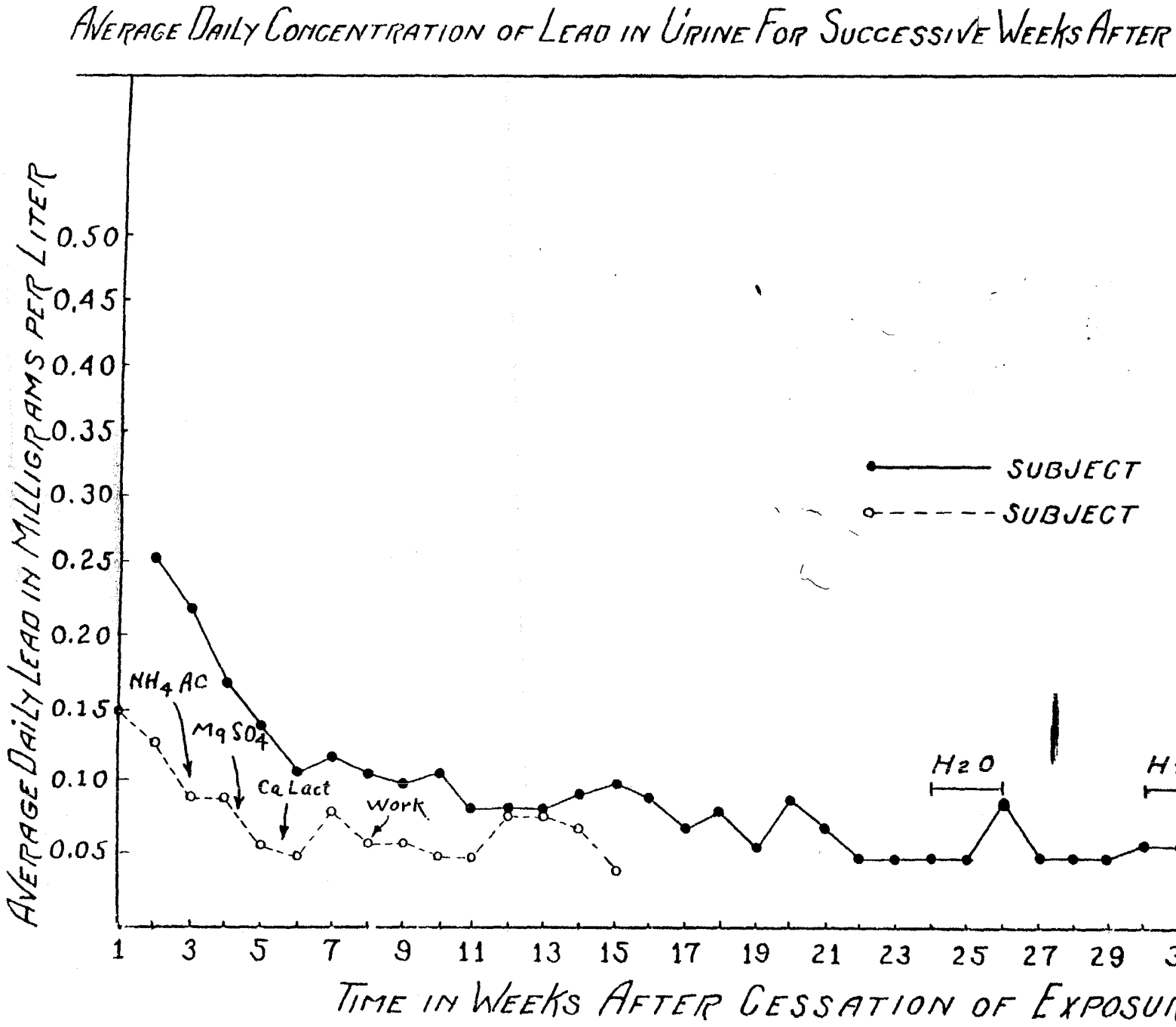

AVERAGE DAILY OUTPUT OF LEAD IN URINE FOR SUCCESSIVE WEEKS AFTER
AVERAGE DAILY LEAD IN MILLIGRAMS
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
SUBJECT
SUBJECT
NH4AC
MgSO4
CaLact
WORK
H2O
H2
1
3
5
7
9
11
13
15
17
19
21
23
25
27
29
TIME IN WEEKS AFTER CESSATION OF EXPOSUR

Daily Output of Lead in Faeces For Successive Weeks After Cessation of Exposure



KEB 01409

Time in Weeks After Cessation of Exposure


AVERAGE DAILY CONCENTRATION OF LEAD IN URINE FOR SUCCESSIVE WEEKS AFTER
AVERAGE DAILY LEAD IN MILLIGRAMS PER LITER
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
SUBJECT
SUBJECT
NH4 AC
MgSO4
Ca Lact
Work
H2O
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29
TIME IN WEEKS AFTER CESSATION OF EXPOSU

Because of the lead intoxication, the previously neglected luetic condition was permitted to go untreated until such a time as it could be inaugurated without risk. The first treatment (Salvarsan) was given on the seventy-first day in the laboratory. (Cf. Figure ___ and legend.) No other treatment of any kind was employed during the early months of the study, since the subject was in no distress, and since we wished to observe the lead excretion uninfluenced by any factors of our own making. The diet of the subject was varied and adequate, and entirely of his own choosing. Since food was provided out of experimental funds, the factor of cost did not influence its quality or quantity.

The amount of lead in the first sample of faeces (1.72 mg.) falls far short of what it must have been on the day following the cessation of exposure. The mean figure for the samples of white lead workers similarly exposed was 7.6 milligrams. Attention is called to this fact as a reminder that this subject, seen two weeks after his last workday, could not provide a faecal sample which bore any evidence of the exposure of that day. However, the faecal lead is high, and is subject to wide fluctuations. Beginning on November 18th, and occurring from time to time until the middle of December, a new phenomenon appeared in the faecal excretion, which required some explanation. High results, entirely outside the previous range, and in fact, outside any reasonable excretory range, began to appear. A survey of the diet list revealed a perfect correlation of a meal of fried or stewed rabbit with these occurrences. In order to avoid similar results the subject was warned against the inclusion of game animals of any type in his diet. Such aberrant figures promptly ceased to appear, and were not seen again except on two occasions, one in February (4.40 mg.) and one in March (3.00 mg.). These may have resulted from an unusual amount of lead arsenate on fruit

VE 01411

ingested on these occasions, but no certain explanation can be given The other high points in the faecal excretion are the result of the accumulation of faeces in the alimentary tract during the periods of constipation, which were of frequent occurrence. The trend of the alimentary lead excretion is gradual and unmistakably downward. If the average amounts per week are plotted to form a curve, there is a downward trend over the entire period of thirty-five weeks, with numerous irregularities corresponding to those which are seen in the daily graph. At the end of this time, the faecal excretion corresponds approximately to the level of the faecal excretion of normal persons. Clearly, it cannot have gone appreciably lower. The irregularity of the curve defeats any fine attempts at its interpretation. Nevertheless it is important to note that there is no evidence of a critical break in the level of faecal lead excretion either at the time of disappearance of symptoms (cf. the arrow at December 10th), or at any other time. Undoubtedly, the lead content of the subject's food was a factor in the irregularity of the faecal curve. Despite this disadvantageous factor, it seems to be a reasonable assumption, from the facts, that as the quantity of lead in the tissues diminished, the excretion of lead in the faeces diminished also.

When the urinary excretion is considered, the results are yet more striking. The high level at the start is maintained with only a fleeting dip for two weeks, after which it slowly slopes off, to be elevated again to a remarkable degree by a mere increase in water intake and elimination. After this period it falls to a level which is essentially normal, being slightly raised during a period in which lemonade was administered. The increase in this instance is not definitely higher than would be accounted for on the basis of increased water intake. Again there is no critical point in the

curve, but only a gradual irregular diminution. The period of work at the end of the observations was not sufficiently energetic to demonstrate any certain effect. Nor was it carried out with such uniformity as to establish the negative fact. In fact, it introduce an undesirable factor into the observations, from the point of view of the subject, and to such an extent that relations which had been mutually cordial and beneficial became somewhat strained. When this situation developed the study was abruptly terminated, since it could be continued with profit only through the perfect coöperation of the subject. By this time, the subject was in excellent health except for the irreversible sequelae of a luetic aortitis, so far as examination indicated his physical state.

The concentration of lead in the blood showed a general correspondence in its behavior to that of the urinary excretion. It is particularly noteworthy that during the period of high water intake the amounts of lead in the blood were too small to be detected by the methods employed. This is precisely what would be expected if the greater lead output in the urine was produced by the simple leaching out of soluble lead, rather than by an interference with the mechanisms of lead distribution in the tissues.

The occurrence of basophilic stippling of the erythrocytes during the study is in strict relationship to the other observations except that it disappears at a much earlier date than do the other abnormal findings. It reaches an approximately normal level at the time subjective symptoms vanish. From this fact one might attribute an unwarranted importance to the phebomenon, but in consideration of the frequency of occurrence of high findings in persons who have no symptoms or signs of intoxication, the significance of the drop in this instance must be left to speculation.

LE 01413

Legend for Figure ___ (Smith)

The daily excretion of lead in the faeces is plotted on the lower curve, the cross-hatched portion indicating the amounts found by analysis, the solid black representing lead in milligrams per gram of ash.

The daily urinary lead excretion in the amounts ~~as~~ found by analysis is in solid black in the upper curve. The stippled areas refer to the volume of urine voided.

The topmost solid black areas are set down on the dates on which 50 c.c. blood samples were obtained. The projection of these blocks below the top line, expresses lead in the blood, in milligrams per 100 c.c., on the same scale as the urinary lead is plotted.

The number of stippled erythrocytes found in fifty fields of the daily smears are shown by the dots on the broken line curve. The zero point of this curve is represented by the continuous straight line which extends across the lower (faecal) curve.

At certain points where amounts go beyond the upper limits of the curve the amount of the item in question is inserted in numbers.

Any lost samples are so recorded. The absence of records on other days are due to failure of alimentary evacuation.

Days marked ⊃ at the top of the faecal curve are those on which the subject ingested fried or stewed rabbit.

The days similarly marked ⊹ are those on which a treatment with salvarsen was adminixtered, in the treatment of previously neglected syphilis.

ILE 01414

The value of the facts displayed in the study of the foregoing subject in the diagnosis and treatment of lead poisoning may be left for later consideration. For the present, let us deal only with their significance in the clarification of the factors which influence the magnitude of lead excretion. It has been shown that lead excretion varies with the extent of daily lead exposure. It may now be recognized that it also depends upon the amount of lead which has been absorbed into the tissues. An objection to this conclusion may be raised to the effect that the subject was not necessarily typical or normal, in that he had a disease (syphilis) which may have influenced the results. That this was not the case is shown by similar observations on another subject, a young, apparently healthy negro, whose exposure had been brief but severe.

This subject, years of age, had been employed in a white lead plant for . Impending unemployment brought him into our hands when we were in search of a suitable subject. He came to the laboratory directly after a day's work and after a physical examination he was accepted as satisfactory for our purposes. The significant items of his physical examination include

Figure ___ shows the results of four months of daily observations. A number of samples of faeces, and two samples of urine were lost in the first and second weeks, for a variety of reasons, but there were no difficulties thereafter. The subject proved to be a reliable and coöperative participant in the experiment.

KE 01415

In certain notable respects Figure ___ differs from Figure ___ . The faecal curve in Figure ___ begins with a high point, followed by an immediate large drop, after which the initial level is never regained. This is a characteristic effect of the abrupt cessation of exposure to lead dusts, the result of the swallowing of lead deposited in the upper respiratory passages on the previous day being apparent in the faeces. From this point on the amounts of lead appearing in the faeces of this subject are smaller than those in the corresponding period of the observations made on the other subject. This, in itself is significant, for the exposure of the two men was of the same type and presumably of approximately the same intensity. In the first case, however, it was prolonged, while in this subject it was of short duration. Presumably a smaller amount of lead accumulated in the tissues during the shorter exposure, and there is a corresponding diminution in the rate of excretion. There is a further difference in that there is a more gradual slope to the curve of diminishing faecal lead excretion. Unfortunately the observations were not continued until the normal level was reached, and it is impossible, therefore, to compare the two subjects in this regard. (It is of considerable practical importance to note that the evidence of significant exposure persisted for four months.) Despite the differences in the faecal excretion as represented in the two figures, the general facts are in correspondence. There is a gradual decrease in the magnitude of the daily excretion, and there is no critical change at any point. In fact, the various experimental efforts to influence the rate of excretion as recorded on the curve, have had little or no clearly demonstrable effect, with the exception of magnesium sulphate, which was certainly responsible for the elimination of an increased amount of lead, with the increased activity of the

LE 01416

alimentary tract, on the first day of the treatment. This was administered in four doses daily, at four hour intervals, each dose consisting of five grams of $MgSO_4.8H_2O$ dissolved in a minimal quantity of water.

Check this in original data.

The urinary graph shows much the same general trend as does that of the faeces. Two peaks of unusual magnitude occur on the eighth and thirteenth days respectively, coincident with the ingestion of abnormal amounts of water. The other irregularly spaced high points or low points have no necessary relation to the materials administered at various times as indicated, since similar high and low points occur elsewhere without relation to treatment. It is especially interesting to note that the administration of calcium lactate in four doses of two grams each at four hour intervals over a period of four days failed to cause an appreciable drop in the excretory rate. The biliary drainages on the seventy-first and eighty-fourth days respectively served only to demonstrate the presence of measureable amounts of lead in the bile.

Check amts. in original data.

The lead in the blood of this subject was less in amount than that found in the blood of the first subject for a corresponding period. However, just as the lead excretion failed to reach a normal level, so the blood failed to reach a point where consistently negative results were obtained.

The observations as to the occurrence of stippling of erythrocytes were ~~made~~ somewhat irregularly. They require no comment.

KE ■ 01417

6. Summary and Discussion

The results of the full ~~the~~ ~~studies~~ ~~established~~ of the lead excretion of groups of workers in the lead trades both under conditions of exposure to lead, and after the cessation of exposure, justified an attempt to ~~establish~~ arrange the solvent ~~points~~ which have been established.

1927	2.0 cc	3.0%	.82
1928	1.75 cc	5.28%	5.4
1929	1.62 cc	9.1%	
1930	1.84 cc	12.0%	
1931	1.91 cc	12.0%	.82
1932 x	2.2 cc		

letters of file

26 - 523727

27 - 1,000,604

28 - 1,565,736

29

30

31

68, 000, 600

2.1 cc

1,565,736

527 900,000,000

From the desk of GRAHAM EDGAR

1.75

YE 01418

ETHYL GASOLINE AND ALL GASOLINE SALES IN U.S.

1926 - 1931

Year	Ethyl Gasoline Sales in U.S.	All Gasoline Consumed in U.S.*
1926	79,315,600**	9,075,858,000 (X)
1927	288,484,450	9,437,188,000
1928	527,803,050	10,698,787,000
1929	1,241,416,050	13,549,879,000
1930	1,854,505,900	15,759,039,000
1931	1,970,389,463	16,416,705,000

* Figures for All Gasoline Consumption reported by A.P.I. do not include-
Ill. for 1927,1928,1929.
Mass.,N.Y. for 1928.
N.Y. (Jan.through April) 1929.
N.J. (Jan.through June) 1927.

** This figure includes only Ethyl Gasoline sold from Sept. through Dec. 1926. The record of 1926 Ethyl Gasoline Sales is incomplete.

(X) Last 4 months 3,136,049,000

VE 01419

Chapter VI

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

1. The Nature of the Lead Hazards

The development of a motor fuel containing tetraethyl lead rais certain questions in industrial and public health which have claimed an unusual amount of attention. In an early stage of the new commerci enterprise it became apparent that the manufacture of tetraethyl lead and the blending of the concentrated fluid employed in the preparation of the commodity known as Ethyl Gasoline, was an hazardous occupation which furnished 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 apparently persisted in many minds. Therefore the distinction between them must be made clear.

Pure tetraethyl lead is a heavy, colorless, oily liquid which is peculiarly difficult to retain within jointed receptacles 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 property it penetrates the unbroken skin of animals. Indeed skin absorption alone may result in the rapid production of acute illness and death in experimental animals From a purely physical point of view, the volatility of tetraethyl lead is low, but considered in toxicological terms it is dangerously high, since at ordinary temperatures air saturated with its vapor contains approximately five milligrams of lead (as Pb) per liter. This concentration is lethal for experimental animals (rabbits) in a few hours, 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 sharp 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 tetraethyl lead emerged from a laboratory scale into an incipient commercial stage requiring factory facilities, cases of lead poisoning of the most serious type occurred, ~~associated with~~ characterized by the sudden onset of cerebral symptoms and ~~with~~ resulting in a high mortality.

Without entering into an irrelevant description of the various steps by which Ethyl Gasoline is prepared for the market, suffice it to say that the hazards of the manufacturing processes are inseparably associated with the characteristics of tetraethyl lead described above. The hygienic problem at every point consists in the prevention of skin contact with tetraethyl lead on the part of workmen, and in the maintenance of conditions under which the vapor of tetraethyl lead is not present in the air breathed by workmen. Because of the sharp localization of the dangers, they are amenable to exact and adequate control; nevertheless the potential hazards are great, so that safety is maintained only by continual vigilance in the prevention of accidents and in the avoidance of careless practices.

The hazards associated with the handling and use of the finished product, Ethyl Gasoline, differ both in quality and quantity from those

which lurk 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 Ethyl Gasoline to produce a [redacted] substantiated case of lead intoxication in the the nine and a half years of its continuous use, up to the present (July, 1932), in certain parts of the 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 Ethyl Gasoline, are so varied and so widespread as to defy regulation. But there are other points of difference which have not required the test of experience for their recognition. Ethyl Gasoline contains tetraethyl lead in amounts so small that the solution has lost the essential toxicological properties of tetraethyl lead. Thus, whereas tetraethy lead alone, or in high concentration in gasoline, is absorbed through the skin rapidly, its absorption is retarded greatly by dilution in gasoline. Indeed we have been unable to obtain evidence of appreciable lead absorption through the skin of experimental animals after their prolonged exposure to concentrations of one part of tetraethyl lead per thousand parts of gasoline, by volume.[2] The importance of this fact is two-fold. Not only does it indicate the improbability of the absorption of lead out of

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* Footnote: Among the thousands of persons in the United States engaged in the handling of Ethyl Gasoline or otherwise exposed to its possible dangers, ~~fewer than one hundred~~ cases of real or supposed injury, have come to the knowledge of the author. Most of these have had no relationship to lead absorption. Only three have ~~had a sufficient degree of clinical resemblance to cases of lead intoxication, to be regarded as questionable.~~ ~~Careful study of these cases failed in each instance to establish a satisfactory basis for the diagnosis of lead poisoning.~~

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gasoline on the part of persons who come in contact with Ethyl Gasoline, but it also establishes the certainty that any minute amount of lead which might be absorbed would be unable to distribute itself in the fatty tissues and the nervous system in the manner characteristic of tetraethyl lead when absorbed at a rapid rate.[2] An equally important effect of the dilution of tetraethyl lead with gasoline is the elimination of the danger of inhalation of lead, to a very large extent. 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 ~~detectable amounts of~~ lead can be found in the vapor. It follows, ~~from this fact~~ therefore, that the vapors rising from tanks containing Ethyl Gasoline do not contain ~~detectable~~ appreciable amounts of lead. However, this does not mean that no tetraethyl lead is evaporated under any of the practical conditions of handling and use or spillage of Ethyl Gasoline.

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

Ethyl 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 and on the European Continent, a large amount of gasoline is distributed in two-gallon cans which are filled by essentially automatic machines at refineries and at storage points. Large numbers of persons

come in contact with Ethyl Gasoline to a greater or lesser degree through spillage, as an unavoidable result of the various methods of distribution. They also inhale vapors from tanks, hose lines and from 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 Ethyl Gasoline may bring about the accumulation of higher boiling petroleum fractions, and of 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.

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 much 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 considerable 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 Ethyl 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 Ethyl 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 further means of contaminating his hands, his clothing and his surroundings. ~~The accumulation of lead dust within the garage as a result of these factors, together with the settling of the lead of the exhaust gas, is likely to be greatly exceeded by that which originates from the repair of electrical storage batteries, the use of paints and solder, and from such similar practices which are carried out commonly in the repair of automobiles. Nevertheless~~ we must regard ~~them as contributors, albeit hypothetically, to the deposits~~ of lead ~~which may be picked up by air currents and mixed into the air~~ [illegible]

One further point must be considered in a complete analysis of the potential public health hazards of 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.

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The qualitative character of the lead hazards derived from the use of Ethyl Gasoline is based upon the methods of its distribution and use. The general magnitude of these hazards is dependent upon the extent of the distribution of Ethyl 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. Accordingly a complete representation of the situation requires some attention to these details.

Ethyl Gasoline 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 around Dayton and Cincinnati. 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 Ethyl 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 this time Ethyl 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 in which it first appeared on the market, - viz., in the cities of Dayton, Cincinnati, Savannah, Jacksonville and Atlanta and their vicinities. The resumption of distribution in 1926 resulted in the rapid expansion of the area over which the fuel was used. This expansion continued until Ethyl Gasoline had become available in all parts of the United States. Table 1 demonstrates the spread in the distribution in terms of 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 of Ethyl Gasoline sold during the years for which

TABLE I

Period of Distribution of Ethyl 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, Ohio	April 1923	none	6.5
Wheeling, W.Va.	Summer 1923	May 1925 to Summer 1926	3.2
Chicago, Ill.	Autumn 1923	~~same~~	3.2
Detroit, Mich.	Autumn 1923	~~same~~	3.2
St. Louis, Mo.	Spring 1924	~~same~~	3.2
Kansas City, Mo.	Spring 1924	~~same~~	3.2
Minneapolis, Minn.	Spring 1924	~~May 1925 to~~ June 1926	3.2
Milwaukee, Wis.	Spring 1924	~~same~~	3.2
Baltimore, Md.	Spring 1924	~~same~~	3.2
Washington, D.C.	Spring 1924	~~same~~	3.2
San Antonio, Texas	Spring 1924	~~same~~	3.2
Savannah, Ga.	Autumn 1924	none	5.0
Atlanta, Ga.	Autumn 1924	none	5.0
Jacksonville, Fla.	Autumn 1924	none	5.0
New Orleans, La.	Summer 1926	none	3.2
Cleveland, Ohio	Summer 1926	none	3.2
Philadelphia, Pa.	Summer 1926	none	3.2
Boston, Mass.	Summer 1926	none	3.2
Denver, Colo.	Summer 1926	none	2.2
San Francisco, Cal.	Summer 1927	none	2.2
Los Angeles, Cal.	Summer 1927	none	2.2
Spokane, Wash.	Summer 1927	none	2.2
Tulsa, Okla.	Summer 1927	none	2.2
New York City	Autumn 1928	none	1.0

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figures are available are shown in Table 2. It should be noted that the general areas into which Ethyl Gasoline was first introduced have maintained the largest proportional and gross consumption.

The concentration of tetraethyl lead in gasoline up to 1926 was maintained at three cubic centimeters per gallon - approximately one part of tetraethyl lead in thirteen hundred parts of gasoline, by volume. 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 three cubic centimeters 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 conception of the proportions of the problem which confronts us.

It is not to be supposed that the possibilities of danger in the general use of Ethyl Gasoline have gone unnoticed up to the present time. On the contrary, numerous experimental inquiries have been carried out. Thus the United States Bureau of Mines began an investigation of the hazards associated with the exhaust gas of automobiles employing Ethyl Gasoline as a fuel, in the autumn of 1923, before the new fuel had developed more than a localized distribution. The further investigations of the Bureau of Mines extended over other phases of the question. The United States Public Health Service studied the matter in 1925, and the Ministry of Health of Great Britain critically reviewed the previous experimental work and made further contrubutions to it in 1928. Each of the latter two governmental agencies acted under the guidance of its own committee of experts appointed especially for that purpose. Our own

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

Distribution Areas of the United States	1926		1927		1928		1929 (6 months)	
	Millions of Gallons of Ethyl Gasoline.	Percentage of Ethyl Gasoline to Total Gasoline	Millions of Gallons of Ethyl Gasoline.	Percentage of Ethyl Gasoline to Total Gasoline.	Millions of Gallons of Ethyl Gasoline	Percentage of Ethyl Gasoline to Total Gasoline.	Millions of Gallons of Ethyl Gasoline.	Percentage of Ethyl Gasoline to Total Gasoline.
New England States and New York.	8.0	0.5	52.0	3.2	91.0	4.9	87.0	4.4
Pennsylvania	5.0	0.9	30.0	4.4	75.0	9.9	85.0	10.4
Atlantic Coast States	7.0	0.7	6.0	0.6	18.0	1.4	92.0	6.8
Ohio	1.0	0.15	16.0	2.1	93.0	10.8	150.0	17.0
Kentucky, Georgia, Florida. Mississippi Alabama	3.0	0.36	18.0	1.9	39.0	3.7	53.0	5.1
Louisianna Arkansas, Tennessee	0.5	0.2	0.5	0.2	8.0	2.9	53.0	19.3
Central States	25.0	0.8	110.0	3.3	172.0	4.9	244.0	6.5
Texas, Oklahoma	0.8	0.1	4.0	0.5	8.0	0.8	13.0	1.4
Rocky Mt. States	2.5	0.8	10.0	3.1	16.0	4.3	20.0	5.5
West Coast States	0.0	0.0	30.0	2.1	27.0	1.8	40.0	2.5
TOTAL	52.8	0.58	276.5	2.5	547.0	4.4	837.0	6.5

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TABLE 3

Average Tetra-ethyl Lead Content of Ethyl 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 G			
	1926	1927	1928	1929
New England States and New York	1.1	1.1	1.2	0.9
Pennsylvania	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, Mississippi, 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, 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	1.3	1.5

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observations, beginning in 1924, have dealt with several aspects of the problem. First in 1925, and successively in 1926 and 1927, we investigated the lead exposure of persons engaged in the handling of Ethyl Gasoline and in the repair of automobiles using Ethyl Gasoline as a fuel. These have been described in detailed reports [1] to the United States Public Health Service, and to the Ethyl Gasoline Corporation, whose officials sponsored the work. The fourth of such field investigations is the subject of the paragraphs which are to follow. I shall not discuss the methods or the results of the earlier experimental work carried out by ourselves or others, except to point out that none of them disclosed evidence of danger either to the health of persons engaged in the handling of Ethyl Gasoline or to that of the general public. In the light of the ~~knowledge~~ which they have furnished, there can be little doubt that some of the hypothetical hazards which have been described, do not exist. However, I shall disregard such considerations for present purposes and shall confine myself to the presentation of observations which were made in the autumn and winter of 1929-30, employing certain items of our earlier data only for purposes of comparison. ~~These~~ observations had ~~the purpose of providing~~ an answer to one question. - Is the magnitude of lead exposure arising from the combined hazards of the use of Ethyl Gasoline such as to bring about appreciable lead absorption on the part of any group of individuals in the community? In terms of the facts presented in previous pages of this volume, this question should be answered adequately through the study of groups of persons who have had the severest and longest exposure to such lead hazards. Accordingly, groups of subjects have been selected for detailed study of the effects of their occupation upon their health, and upon such physiological processes as are specifically influenced by a significant increase in lead absorption.

2. The Selection of Experimental Subjects.

Table 4 shows the numbers and types of subjects selected, together with the locality in which they were employed. The three groups of workmen who experience all means of exposure to the possible hazards associated with the use of Ethyl Gasoline are adequately represented by fifty-six filling station attendants, fifty tank-truck handlers of such gasoline, and two hundred and one 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 Ethyl Gasoline for the longest period of time, who had handled gasoline containing the highest concentrations of tetraethyl lead, and who handled the largest amounts of Ethyl Gasoline daily, were especially desirable. Until May of 1935 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 hazards 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 Ethyl Gasoline since its introduction on the market. Furthermore the employment turnover of filling station attendants had been so slight that it was not difficult to find a satisfactory group of men who had dispensed Ethyl Gasoline since it was first marketed from their stations.

The consumption of Ethyl Gasoline had 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

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TABLE 4

DISTRIBUTION OF SUBJECTS ACCORDING TO OCCUPATION A D LOCALITY

Locality	Number of Filling Station Attendants Exposed to Ethyl Gas. #1 - # 56	Number of Tank Wagon Handlers Exposed to Ethyl Gas. #101-#150	Number of Garage Mechanics Exposed to Ethyl Gas. 301-#501	Number of Barrel Fillers Not Exposed to Ethyl Gasoline #201 -#227	Number of Barrel Fillers Exposed to Ethyl Gasoline #251 - #272
Cleveland Ohio			15		
Cincinnati Ohio	11	1	13		
Dayton Ohio	11	10	15		
Chicago Illinois	6	9	13		
Detroit Michigan	1	11	12		
St. Louis Missouri	11	8	48		
Kansas City Missouri	~~0~~	1	5		
Minneapolis Minnesota	~~0~~		5		
Jacksonville Florida	6	6	5		
Atlanta Georgia	10	4	5		
Milwaukee Wisconsin			5		
Boston Mass.			50		
Wheeling W. Va.			10		
New York New York				27	22
Total	56	50	201	27	22

well located filling stations had handled more Ethyl Gasoline than had similarly employed men 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 Ethyl Gasoline. Twenty-seven 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 is made up of one hundred and nine persons who have been working on cars which used only Ethyl Gasoline, and an additional ninety-three who have 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 Ethyl 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 Ethyl Gasoline had been the exclusive fuel from 1923 to the time of the present investigation. Thirty-nine subjects had had from three to six years of daily repair work on cars in which Ethyl 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 Ethyl Gasoline. The garage mechanic group is entitled to special consideration since it is composed of men whose occupation combines all of the potential lead exposures derived from Ethyl Gasoline in an intensified form, together with certain other lead exposures which are not related to Ethyl Gasoline. It is for this reason that it was expanded to a large number at the expense of the less exposed groups.

The barrel-fillers referred to in Table 4 were included among the subjects chosen for the present investigation 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 aroused our interest in the influence of repeated and prolonged gasoline absorption. Accordingly search was made for a group of subjects whose exposure to gasoline was severe and uncomplicated by other factors. In the summer of 1923 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 vapors. In addition, the skin, clothing and shoes of workmen were frequently and almost continuously soaked 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 faeces. (These latter data [illegible])

[illegible]

Shortly after these examinations had been completed the refinery in question embarked upon the distribution of Ethyl 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

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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 situation from the point of view of severity of exposure. Therefore it was considered imperative to obtain information which would show whether or not an appreciable lead absorption was occurring in the men. Accordingly, at the end of a period of six months, during which Ethyl Gasoline had been handled daily in this manner, the workmen so employed were examined, and samples of their excreta were obtained for analysis. In the second group made up of twenty-two 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 Ethyl Gasoline, were not obtained for study. At the time of the present study of filling station employees, tank wagon handlers of Ethyl Gasoline and garage mechanics, there was no area of the United States in which the selection of entirely unexposed subjects could be made with precision. The use of leaded gasoline had increased rapidly, so as to involve all parts of the country. Furthermore the employees of a large proportion of the major gasoline distributing companies were handling Ethyl Gasoline. Therefore it was necessary to rely on information obtained prior to the general distribution of Ethyl Gasoline, for comparative data on similar groups of subjects independent of the factor of leaded gasoline. Fortunately, such data were adequate. Furthermore, repeated observations had been made on the same individuals under conditions of continuous exposure. These successive findings furnish a means for the discovery of progressive effects of any type.

3. Methods of Study

The facts presented in earlier chapters would seem to establish the relationship between lead excretion and lead absorption. Thus it seems certain that the most specific evidence of the magnitude of lead exposure and absorption is to be found in the rate of lead excretion, in which the faecal 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. Nevertheless considering the importance of the matter at issue, we have considered it desirable to leave no stone unturned which might yield additional information. Accordingly we have searched for clinical evidences of lead absorption with the same care that we have applied to the collection of accurate analytical data. The general clinical methods were similar to those employed by J. P. Leake and his associates and by ourselves in other investigations of the same question. A comprehensive neurological examination constituted the only significant addition to the previous technique.

Care was taken to obtain all the information possible from each subject, and to record such information in a uniform manner. For this reason cards for recording data were provided as reproduced below and the work was divided among four physicians each of whom carried out the same type of observation on each subject. So far as possible quantitative information was obtained in the physical examination, but without the subordination of clinical judgment to the necessities of statistical comparability. Thus while it was recognized that a statistical study of all the data was desirable and necessary, sound 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

HISTORY SHEET

[redacted]

No. Examiner's Initials Date

Name Age Race Color Birthplace

Marital Ages Children Miscarriages Stage

Residence

Other places lived in, with dates

Place of Employment

Type of work (exact description of nature and conditions)

Length of present employment and previous employment at same work

Previous Occupations

Dates

Previous Lead Hazards	Dates	Previous Lead Hazards	Dates
Painting		Brass Founding	
Plumbing		Soldering	
Carriage, Auto or Car		Enameling	
Type Casting		Paint Mfg.	
Smelting or Refining		Pottery	
"Treating" Refineries		Glass	
Storage Bat. Mfg. or Rep.		Polishing Cut Glass	
Lead Burning		White Lead	
Printing or Lithog.		Rubber	
Mining		Garage	
Foil, Solder, Babbit, Mfg.		Telephone or Telegraph Rep.	

Automobile Owner Gasoline Used Repair Work

Previous Illnesses with dates and exact descriptions (no leading questions)

[redacted]

Tbc. Malaria Rheumatism Lues. Gc. Scarlet Diph. Typhoid

Tonsillitis Frequent Colds Convulsions Heart Disease Asthma

Significant Family History:

Remarks:

HISTORY SHEET (cont)

No. Examiner's Initials Date

Sleep Hours in Bed Dreams Restful Disturbed

Bowel Movements Frequency Hour

Tendency to Constipation Cathartics

Tendency to Frequent Stools

Teeth Brushing When Last Trip to Dentist

Usual Weight Best Weight Recent Loss Weight (seasonal?)

General Health

Rate of Tiring Recent Change

Headaches Time

Eye Trouble (character and time of development)

Taste in Mouth Character Time

Pains in Joints Swelling of Joints

Muscular Strength Cramps in Muscles

Pains in Belly Character Frequency

Appetite Different Meals

Digestive Disturbances Nausea or Vomiting

Skin Infection or Eruption General Hands

Polyuria Nocturia Frequency

Nervousness General Weakness

Other Complaints Right or Left Handed

Loss of Strength in Arms or Legs at any time

Shooting pains

Numbness or tingling

Loss of Sensation

PHYSICAL EXAMINATION SHEET

No. Examiner's Init. Date Age Height Weight

General Appearance
Nutrition
Pulse
Temperature

Posture
Musculature
Blood Pressure (seated)

Condition of Skin

Color of Skin (exact)

Condition of Skin of Hands

Cornea

Sclera

Nose

Throat

Glands

Tonsils

Mucous Membranes

Ears (structure)

Teeth

Gums Pyorrhoea

Lead Line (Appearance and Location)

Heart Apex Rate
After 25 hops
2 minutes after

R.C.D. x
R.S.D.

Lungs: K.I. - R.
L.

D.E. - R.
L.

L.L.B. - R.
L.

Chest Diagnosis

Abdomen

Liver Spleen Kidneys

Rectum Genitalia

Upper Extremities Lower Extremities

Diagnosis and Remarks

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NEUROLOGICAL EXAMINATION

Examiner's Init.

Cranial Nerves

1 Smell

11 Sight R - 15/ L - 15/ Condition Correction

111, 1V, V1 Extrinsic Eye Muscles

Pupils Reflexes

Visual Field

V Motor Sensory

V11 Facies

V111 Audition R L Equilibrium

1X, X, X11 Speech Swallowing Tongue

X1 Neck Shoulders

Upper Extremities Reflexes

Tonus
Atrophy
Ataxia
Tremor
Muscular Power
Dynamometer
Stereognostic
Epicritic
Protopathic
Kinaesthetic
Thermal
Vibratory
Nerve Trunk Tenderness

Pharyngeal
Biceps
Triceps
Radial
Patellar
Achilles
Epigastric
Abdominal
Cremasteric
Plantar

Lower Extremities Gait

LABORATORY SHEET

No. Examiner's Initials Date

URINALYSIS:

Quantity

Sp. G.

Reaction (Methyl Red)

Albumin (Heller's) Heat and Acetic

Sugar (Fehling's)

Acetone (Nitroprusside)

Microscopic

BLOOD: White Count Haemoglobin (Dare)

Red Count

Differential (100 cells): Poly. Neutrophiles
Poly. Eosinophiles
Poly. Basophiles
Lymphocytes

Endothelial
Large Mononuclear
Transitional

Abnormal

Polychromasia

Stippling per 50 fields

ANALYTICAL EXAMINATION:

Accurate statement of hours required for collection of:

Urine Faeces

Constipation Diarrhoea Cathartic (type)

FAECES

Wt. dish + dri3d faeces
Wt. dish + ash
Wt. dish
Wt. dried faeces
Wt. ash

lead Mgs.
Mgs./gram of ash
Analysis No.

URINE

Volume c.c.

Lead Mgs.
Mgs./liter
Analysis No.

LE 01443

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 while 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

LABORATORY SHEET

No. Examiner's Initials Date

URINALYSIS:

Quantity

Sp. G.

Reaction (Methyl Red)

Albumin (Heller's) Heat and Acetic

Sugar (Fehling's)

Acetone (Nitroprusside)

Microscopic

BLOOD: White Count Haemoglobin (Dare)

Red Count

Differential (100 cells): Poly. Neutrophiles
Poly. Eosinophiles
Poly. Basophiles
Lymphocytes

Endothelial
Large Mononuclear
Transitional

Abnormal

Polychromasia

Stippling per 50 fields

ANALYTICAL EXAMINATION:

Accurate statement of hours required for collection of:

Urine Faeces

Constipation Diarrhoea Cathartic (type)

FAECES

Wt. dish + dried faeces
Wt. dish + ash
Wt. dish
Wt. dried faeces
Wt. ash

lead Mgs.
Mgs./gram of ash
Analysis No.

URINE

Volume c.c.

Lead Mgs.
Mgs./liter
Analysis No.

UE 01445

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 while 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 only on the barrel-filler group of subjects. Otherwise, such procedures were followed only when indicated for diagnostic purposes.

Haemoglobin determinations were made on each subject by means of the Dare haemoglobinometer. 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 the method previously described.

Samples of urine and faeces were obtained from the subjects for the determination of their lead content. The collection and the analyses were carried out according to the methods detailed in Chapter II. 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 conspicuously absent. Of special negative clinical importance were the complete absence of lead line, the lack of significant microscopic blood changes (stippling), and the striking infrequency of vague symptoms of ill health. In this situation any evidences of significant lead absorption as a consequence of exposure to Ethyl Gasoline must be

sought in the data on the excretion of lead.

The clinical and analytical data for the groups are presented in a series of tables, in which the factors are set down in the exact manner of the statistical study except as otherwise noted.

Table 5 shows the classification of the subjects according to the duration of their exposure to Ethyl Gasoline. One-half of the filling station attendants and a little less than half of the tank wagon handlers had been exposed for five or more years, while sixty-nine percent of the garage mechanics had repaired cars which used Ethyl Gasoline over a period of three 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 to Ethyl Gasoline. None of the garage mechanics may be regarded as free from the possibility of lead exposure in their occupation, apart from the factor of Ethyl 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. 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 eight 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.

TABLE 5

Distribution of Subjects According to Period of Exposure to Ethyl Gasoline

Eliminate the column

Period of Exposure In Years	Filling Station Attendants		Tank Wagon Handlers		Garage Mechanics		Barrel Fillers Not Exposed to Ethyl Gasoline		Barrel Fille Exposed to Ethyl Gasol	
	Number	%	Number	%	Number	%	Number	%	Number	%
0.1-0.25	0	0	0	0	0	0	0	0	4	18
0.5	0	0	0	0	0	0	0	0	18	82
1	1	2	1	2	26	13	0	0	0	0
2	0	0	4	8	36	18	0	0	0	0
3	6	11	4	8	98	49	0	0	0	0
4	16	28	19	38	22	11	0	0	0	0
5	23	41	16	32	12	6	0	0	0	0
6	10	18	6	12	7	3	0	0	0	0
Totals	56	100	50	100	201	100	0	0	22	100

Eliminate all figures

TABLE 4

DISTRIBUTION OF SUBJECTS ACCORDING TO HISTORY OF PREVIOUS EXPOSURE TO LEAD OTHER THAN ETHYL GASOLINE

Description of Lead Exposure	Filling Station Attendants		Tank Wagon Handlers		Garage Mechanics		Barrel Fillers Not Exposed to Ethyl Gasoline		Barrel Fillers Exposed to Ethyl Gaso.	
	Number	%	Number	%	Number	%	Number	%	Number	%
None	20	36	18	36	0	0	15	55	10	46
Questionable	8	14	10	20	30	15	8	30	6	27
Slight	28	50	21	42	163	82	3	11	6	27
Moderate	0	0	1	2	8	4	1	4	0	0
Severe	0	0	0	0	0	0	0	0	0	0
Total	56	100	50	100	201	100	27	100	22	10

Eliminate the next-to-last line

KE 01450

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.

Tables 8 and 9 represent the frequency of occurrence of certain subjective and objective abnormalities which are indicative of the presence of low grade intoxication. Among the symptoms, attention should be called to the high incidence of headache among the garage mechanics. The histories clearly suggested carbon monoxide absorption as the background of this complaint. Irritation of the skin of the hands due to frequent contact with petroleum products showed a high frequency of occurrence in all the groups. Pallor was most prominent in the garage mechanic group and in the barrel fillers not exposed to Ethyl Gasoline. The explanation of this ~~situation~~ in the latter group is undoubtedly ~~due to~~ the fact that this group was examined in the summer when the inhalation of gasoline vapor was at its height. These men showed a correlative diminution in haemoglobin and a high average stippling — further indications of blood changes resulting from their exposure. Comparison of the remaining items with the results of similar observations on various groups of subjects unexposed to Ethyl Gasoline fails to yield any significant information. (Cf. Tables 14 and 20 on pages 51 and 52.)

In Tables 10, 11, and 12, the findings as regards blood pressure ~~taken with subjects seated~~, 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 re-

TABLE 7

Distribution of Subjects According to Age

Age In Years	Filling Station Attendants		Tank Wagon Handlers		Garage Mechanics		Barrel Fillers Not Exposed to Ethyl Gasoline		Barrel Fil Exposed to Ethyl Gaso	
	Number	%	Number	%	Number	%	Number	%	Number	%
15-19	0	0	0	0	9	4	0	0	0	0
20-24	3	5	0	0	32	16	0	0	1	5
25-29	12	21	15	30	33	17	6	23	2	9
30-34	12	21	7	14	34	17	5	19	6	27
35-39	5	9	10	20	42	21	5	19	2	9
40-44	2	4	5	10	26	13	6	23	7	31
45-49	5	9	5	10	11	5	1	4	2	9
50-54	4	7	3	6	8	4	1	4	0	0
55-59	7	13	1	2	4	2	2	8	1	5
60-64	6	11	3	6	2	1	0	0	1	5
65-69	0	0	1	2	0	0	0	0	0	0
Total	56	100	50	100	201	100	26	100	22	100
Mean	40.8		38.6		34.3		37.9		39.1	
Probable Error of Mean	± 1.2		±1.1		±0.5		±1.2		±1.3	
Standard Deviation	13.07		11.28		9.86		3.76		9.34	

VE 01452

TABLE I

Distribution of Subjects According to Certain Subjective Abnormalities

Type of Abnormality	56 Filling Station Attendants		50 Tank Wagon Handlers		201 Garage Mechanics		27 Barrel Fillers Not Exposed to Ethyl Gasoline		22 Barrel Fille Exposed to Ethyl Gasoli	
	Number	%	Number	%	Number	%	Number	%	Number	%
Recent Loss of Weight	3	6	2	4	7	4	0	0	0	0
Increased Tendency to Fatigue	1	2	1	2	8	4	2	7	0	0
Frequent Headache	6	10	2	4	31	15	2	7	1	5
Occasional Abdominal Cramp	2	4	2	4	12	6	1	4	1	5
Occasional Digestive Disturbance	3	5	2	4	4	2	1	4	1	5
Occasional Neuritic Symptoms	3	5	0	0	7	3	0	0	1	5
Poor General Health	0	0	0	0	1	1	0	0	0	0

NE 01453

TABLE I

Distribution of Subjects According to Certain Objective Abnormalities.

Type of Abnormality	Filling Station Attendants		Tank Wagon Handlers		Garage Mechanics		Barrel Fillers Not Exposed to Ethyl Gas line		Barrel Filler Exposed to Ethyl Gasoline	
	Number	%	Number	%	Number	%	Number	%	Number	%
Under-nutrition	4	6	2	4	8	4	4	15	2	10
Pallor	2	4	2	4	23	11	8	30	2	10
Irritation of Skin of Hands	11	20	12	24	56	28	16	60	12	54
Lead Line	0	0	0	0	0	0	0	0	0	0
Nerve Trunk Tenderness	6	11	17	34	17	8	3	11	1	5
Tremors	20	36	21	42	71	35	8	39	9	41
Sensory Disturbances	1	2	3	6	4	2	0	0	2	10
Extensor Paresis	1	2	3	6	1	1	0	0	0	0
Atrophy of Upper Extremities	1	2	4	3	9	4	0	0	1	5
Abnormalities of Visual Field	2	4	1	2	0	0	0	0	2	10
Urinary Acidity	20	39	15	33	92	46	1	4	16	73
Albuminuria	0	0	4	9	6	3	0	0	0	0

VE ■ 01454

TABLE 10

Distribution of Subjects According to Systolic Blood Pressure

Blood Pressure Readings	Filling Station Attendants		Tank Wagon Handlers		Garage Mechanics		Barrel Fillers		Barrel Fil	
	Number	%	Number	%	Number	%	Number	%	Number	
80-89	0	0	0	0	1	1	0	0	0	0
90-99	1	2	0	0	4	2	0	0	1	5
100-109	3	5	2	4	16	8	0	0	0	0
110-119	10	18	16	32	52	26	4	15	5	22
120-129	18	32	10	20	62	30	7	26	7	32
130-139	9	16	7	14	36	18	8	30	4	18
140-149	7	12	4	8	18	9	5	18	4	18
150-159	2	4	2	4	5	2	1	4	0	0
160-169	0	0	3	6	4	2	2	7	0	0
170-179	1	2	0	0	0	0	0	0	1	5
180-189	2	4	2	4	2	1	0	0	0	0
o Information	3	5	4	8	1	1	0	0	0	0
Total	56	100	50	100	201	100	27	100	22	100

Mean	130.1	130.4	135.7	134.3	139.1
Probable Error Of Mean	± 1.7	± 1.9	± 0.7	±1.8	± 2.3
Standard Deviation	17.86	19.30	15.10	13.59	15.86

01455

TABLE II

Distribution of Subjects According to Haemoglobin in Blood

Haemoglobinometer Reading (Dare)	Filling Station Attendants		Tank Wagon Handlers		Garage Mechanics		Barrel Fillers Not Exposed to Ethyl Gasoline		Barrel Fill Exposed to Ethyl Gasol	
	Number	%	Number	%	Number	%	Number	%	Number	%
60 - 67	Ø	Ø	1	2	Ø	Ø	9	33	1	5
68 - 75	15	27	4	8	13	6	12	44	1	5
76 - 83	21	37	12	24	77	39	4	15	8	35
84 - 91	15	27	27	54	92	46	1	4	11	50
92 - 99	5	9	5	10	15	7	Ø	Ø	1	5
No Information	Ø	Ø	1	2	4	2	1	4	Ø	Ø
Total	56	100	50	100	201	100	27	100	22	100
Mean	80.9*		85.0*		84.5*		71.1*		83.3*	
Probable error of Mean	± 0.67		± 0.59		± 0.24		± 0.92		± 0.91	
Standard Deviation	7.39		6.1		5.09		6.98		6.34	

* All means calculated on a wider grouping of readings.

KE ■ 01456

TABLE 12

Distribution of Subjects According to Stippling of Erythrocytes

Number of Stippled Cells Per 30 Fields	Filling Station Attendants		Tank Wagon Handlers		Garage Mechanics		Barrel Fillers Not Exposed to Ethyl Gasoline		Barrel Fill Exposed to Ethyl Gasol	
	Number	%	Number	%	Number	%	Number	%	Number	%
0	36	64	33	66	159	79	7	26	21	95
1	6	11	8	16	19	9	1	4	1	5
2-5	6	11	5	10	17	8	6	22	0	0
6-10	3	5	2	4	5	3	3	11	0	0
11-20	3	5	1	2	1	1	4	15	0	0
21-32	2	4	1	2	0	0	6	22	0	0
Total	56	100	50	100	201	100	27	100	22	10

KGB 01457

lation to Ethyl Gasoline exposure, since practically all the findings are within normal limits. In the case of the systolic blood pressure, which is used here only as a general means of pointing out the probable existence of vascular disease, the high readings are sharply correlated with age, and hence have no significance. The low results are of no ~~higher~~ frequency than is common among corresponding groups of presumably normal persons. The haemoglobin determinations show only a high frequency of low results among the barrel-fillers unexposed to Ethyl Gasoline, as previously pointed out. Likewise the only point of interest in Table 2 is the relatively high results among these same barrel fillers. Apparently, exposure to gasoline vapors may produce blood changes, including the appearance of stippling.

Tables 3 and 4 record the observations on the strength of the grip of the left hand and right hand, respectively, of the subjects. The frequencies and the means do not show any very striking differences between the groups, except ~~to indicate~~ that the barrel fillers as a whole, gave a somewhat weaker response to the test.

The facts obtained from the analysis of the excreta of the subjects are presented in Tables , , and . A survey of the tabulated results shows that a few high results are scattered irregularly through the data.

Where these occur in faecal samples 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. Accordingly the inclusion of such findings in the computation of mean values increases appreciably the probable error

TABLE 13

Distribution of Subjects According to Strength of Grip of Left Hand

Hand Dynamometer Reading	Filling Station Attendants		Tank Wagon Handlers		Garage Mechanics		Barrel Fillers Not Exposed to Ethyl Gasoline		Barrel Fille Exposed to Ethyl Gasoli	
	Number	%	Number	%	Number	%	Number	%	Number	%
50-59	0	0	2	4	4	2	0	0	0	0
60-69	1	2	2	4	3	1	5	19	2	9
70-79	7	12	2	4	8	4	2	7	3	14
80-89	5	9	3	6	30	15	4	15	2	9
90-99	7	12	13	26	47	23	3	11	7	32
100-109	10	18	6	12	42	21	6	22	3	14
110-119	2	4	2	4	20	10	2	7	4	18
120-129	1	2	7	14	25	12	0	0	1	4
130-139	0	0	0	0	5	3	1	4	0	0
140-149	1	2	2	4	5	3	0	0	0	0
150-159	0	0	1	2	1	1	0	0	0	0
160-169	0	0	0	0	2	1	0	0	0	0
No Information	22	39	10	20	9	4	4	15	0	0
Total	56	100	50	100	201	100	27	100	22	100

Mean	95.0	101.5	100.9	91.1	95.0
Probable Error of Mean	±1.9	±2.4	±0.9	±2.7	±2.4
Standard Deviation	16.63	22.75	19.37	19.05	16.51

Exhibit Supplement

KE 01459

TABLE 14

Distribution of Subjects According to Strength of Grip of Right Hand

Hand Dynamometer Reading	Filling Station Attendants		Tank Wagon Handlers		Garage Mechanics		Barrel Fillers Not Exposed to Ethyl Gasoline		Barrel Fil: Exposed to Ethyl Gaso	
	Number	%	Number	%	Number	%	Number	%	Number	%
50-59	0	0	0	0	0	0	2	7	0	0
60-69	0	0	0	0	1	1	0	0	1	4
70-79	0	0	2	4	3	2	3	11	0	0
80-89	3	5	4	8	9	4	1	4	7	33
90-99	8	14	6	12	29	14	4	15	2	9
100-109	4	8	7	14	40	20	3	11	2	9
110-119	7	12	5	10	28	14	5	18	4	18
120-129	5	9	6	12	33	16	3	11	3	14
130-139	3	5	5	10	22	11	1	4	2	9
140-149	2	4	2	4	19	10	1	4	1	4
150-159	1	2	2	4	7	3	0	0	0	0
160-169	0	0	1	2	1	1	0	0	0	0
No Information	23	41	10	20	9	4	4	15	0	0
Total	56	100	50	100	201	100	27	100	22	100

Mean	112.6	114.0	116.3	101.9	105.0
Probable Error of Mean	± 2.2	±2.4	±0.9	±3.3	±3.0
Standard Deviation	18.43	22.34	19.58	23.30	20.89

KE 01460

TABLE 15

45

Distribution of Subjects According to Lead Found in Faeces

Milligrams of Lead Per Sample of Faeces	Filling Station Attendants		Tank Wagon Handlers		Garage Mechanics		Barrel Fillers Not Exposed to Ethyl Gasoline		Barrel Fil Exposed to Ethyl Gaso	
	Number	%	Number	%	Number	%	Number	%	Number	%
0 - 0.079	6	11	1	2	5	3	2	7	0	0
.08- 0.159	5	9	4	8	26	13	4	15	2	9
.16- 0.239	12	21	4	8	33	17	2	7	9	41
.24- 0.319	4	7	6	12	25	12	3	11	5	23
.32- 0.399	8	14	6	12	28	14	4	15	1	5
.40- 0.479	2	4	2	4	17	9	3	11	2	9
.48- 0.559	2	4	5	10	13	6	1	4	1	5
.56- 0.639	1	2	2	4	8	4			0	0
.64- 0.719	0	0	1	2	7	3	3	11	0	0
.72- 0.799	0	0	0	0	7	3	0	0	0	0
.80- 0.879	1	2	0	0	3	2	0	0	1	5
.88- 0.959	0	0	0	0	2	1	1	4	0	0
.96- 1.039	0	0	1	2	2	1	1	4	0	0
1.04- 1.119	0	0	0	0	0	0	0	0	0	0
1.12- 1.199	0	0	0	0	0	0	0	0	0	0
1.20- +	2*	4	1*	2	6*	3	0*	11	1*	5
No information	13	23	17	34	13	6	0	0	0	0
Total	56	100	50	100	201	100	27	100	22	100
Mean	0.258		0.360		0.379		0.380		0.238	
Probable Error of Mean	+0.018		+0.023		+0.012		+0.037		+0.024	
Standard Deviation	0.169		0.197		0.245		0.266		0.160	

KE 01461

TABLE 16

Distribution of Subjects According to Lead in Milligrams per Gram Ash of Faeces

Milligrams of Lead Per Gram of Ash	Filling Station Attendants		Tank Wagon Handlers		Garage Mechanics		Barrel Fillers Not Exposed to Ethyl Gasoline		Barrel Fil Exposed to Ethyl Gaso.	
	Number	%	Number	%	Number	%	Number	%	Number	%
0 0-0.039	10	18	2	4	5	2	1	4	0	0
0.04-0.079	14	24	16	32	51	25	9	33	7	32
0.08-0.119	9	16	4	8	54	27	7	26	8	36
0.12-0.159	4	8	3	6	36	18	3	11	2	9
0.16-0.199	2	4	3	6	18	9	2	7	3	14
0.20-0.239	1	2	1	2	8	4	1	4	2	9
0.24-0.279	1	2	1	2	4	2	1	4	0	0
0.28-0.319	1	2	0	0	4	2	0	0	0	0
0.32-0.359	0	0	0	0	1	1	1	4	0	0
0.36-0.399	0	0	0	0	0	0	0	0	0	0
0.40-0.439	0	0	1	2	0	0	2	7	0	0
0.44-0.479	0	0	0	0	5	2	0	0	0	0
0.48-0.519	0	0	0	0	0	0	0	0	0	0
0.56-0.599	0	0	1	2	0	0	0	0	0	0
0.64-0.679	0	0	0	0	3	1	0	0	0	0
1.00- +	1*	2	1*	3	1*	1	0	0	0	0
No Information	13	22	17	34	13	6	0	0	0	0
Total	56	100	50	100	201	100	27	100	22	100
Mean	0.087		0.120		0.123** 0.131		0.137		0.113	
Probable Error of Mean	± 0.007		± 0.014		± 0.004** ± 0.005		±0.014		± 0. 007	
Standard Deviation	0.065		0.115		0.074** 0.100		0.106		0.052	

*Excluded in Calculation of Mean

01462

** Calculated after exclusion of three

TABLE / 7

Distribution of Subjects According to Milligrams of Lead Per Liter of Urine

Milligrams of Lead Per Liter of Urine	Filling Station Attendants		Tank Wagon Handlers		Garage Mechanics		Barrel Fillers Not Exposed to Ethyl Gasoline		Barrel Fill Exposed to Gasoline	
	Number	%	Number	%	Number	%	Number	%	Number	%
0-0.039	18	32	11	22	45	22	6	22	8	36
.04-0.079	15	27	18	36	76	38	16	60	10	45
.08-0.119	13	23	4	8	34	17	5	18	2	9
.12-0.159	3	5	1	2	16	8	0	0	1	5
.16-0.199	3	5	1	2	5	2	0	0	0	0
.20-0.239	1	2	0	0	3	1	0	0	0	0
.24-0.279	0	0	1	2	3	1	0	0	0	0
.28-0.319	0	0	1	2	3	1	0	0	0	0
.32-0.359	0	0	1	2	1	1	0	0	0	0
.36-0.399	0	0	0	0	1	1	0	0	0	0
.40-0.439	0	0	0	0	1	1	0	0	0	0
.44-0.479	0	0	0	0	1	1	0	0	0	0
.48-0.519	0	0	1	2	1	1	0	0	0	0
.52- +	1**	2	1**	2	3**	1	0	0	0	0
No Information	2	4	10	20	8	4	0	0	1	5
Total	56	100	50	100	201	100	27	100	22	100

Mean	0.071	0.089	0.086	0.058*	0.052*
Probable Error of Mean	±0.005	±0.011	±0.004	±0.009	± 0.004
Standard Deviation	0.050	0.099	0.079	0.071	0.030

* Mean calculated on a wider grouping of findings
** Excluded in calculation of means

01463

of the means. 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 obvious purpose of eliminating a finding which has no possible relation to the problem at issue. In the case of the urine samples, aberrant results are of rare occurence, 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 instructions 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. ~~Thus when a suitably large sample contains as much as half a milligram of lead per liter of urine, one may be certain that lead has been introduced into the sample as a contaminant, unless the subject has absorbed very large amounts of lead shortly before the collection of the sample.~~

The analytical results serve to classify the various groups of subjects as distinctly outside the hazardous lead trades. At first glance, the mean values for the lead content of the faeces of filling station employees, tank wagon handlers and garage mechanics seem high, as compared to normal persons ~~free of~~ occupational lead exposure. (Cf. page) On the other hand, the small group of barrel fillers who were not exposed to Ethyl Gasoline, and who had no other occupational lead exposure at the time of the examinations, show similarly high findings. Furthermore when the faecal lead is expressed in quantitatively comparable terms, in mil igrams per gram of ash, the apparently high results tend to lose their significance. Finally, the previous data have amply demonstrated the impossibility of drawing exact conclusions as to the magnitude of lead absorption,

on the basis of the faecal excretion of lead. Thus it is necessary to resort to the study of the urinary excretion for such information. As judged from this standard, the groups fall into the category of persons lacking occupational exposure to lead compounds.

A special significance derives from the failure of the barrel fillers to show any increase in their lead excretion as a consequence of their exposure to Ethyl 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 ten persons who were examined prior to exposure to Ethyl Gasoline, and again after six months exposure to Ethyl Gasoline, no one person shows an increase in his rate of lead excretion. This can only be interpreted as meaning that there was no significant lead absorption as a consequence of this severe exposure. Thus, it seems quite clear, that the inability of animals to absorb measurable amounts of tetraethyl lead out of gasoline in dilute solution, (1 part per thousand by volume or less) is shared by man.

In view of the important conclusions of the above paragraphs, indicating the completely negative character of the findings, it is only proper to present observations of a strictly comparable character on groups of subjects similar to those employed in the present investigation, in every matter save that of exposure to Ethyl Gasoline. Accordingly, Tables 18 to 24, inclusive show the results obtained in 1927, in the study of groups of persons who had not been exposed to the conditions associated with the use of Ethyl Gasoline. The medical student group differs from that appearing in Tables

TABLE 17

Distribution According to Age of Groups of Subjects Not Exposed To Ethyl Gasoline, Examined in 1927

Age In Years	Medical Students		Filling Station Attendants and Tank Wagon Handlers		Garage Mechanics	
	Number	%	Number	%	Number	%
15-19	11	15	1	1	2	6
20-24	51	72	18	16	2	6
25-29	9	13	23	20	12	34
30-34	0	0	16	14	12	34
35-39	0	0	11	10	2	6
40-44	0	0	13	11	4	11
45-49	0	0	10	9	1	3
50-54	0	0	10	9	0	0
55-59	0	0	5	4	0	0
60-64	0	0	4	4	0	0
65-69	0	0	3	3	0	0
70-74	0	0	0	0	0	0
Total	71	100	114	100	35	100
Mean	22.3		37.5		31.2	
Probable Error Of Mean	±0.2		±0.8		±0.8	
Standard Deviation	2.3		12.54		6.69	

KE 01466

TABLE 14

Distribution According to Certain Subjective Abnormalities of Groups of Subjects Not Exposed to Ethyl Gasoline - Examined in 1927.

Type of Abnormality	71 Medical Students		69 Filling Station Attendants		42 Tank Wagon Handlers		35 Garage Mechanics	
	Number	%	Number	%	Number	%	Number	%
Recent Loss of Weight	7	10	1	1	2	5	5	14
Increased Tendency to Fatigue	9	13	12	17	5	12	5	14
Occasional Headache	15	21	17	25	7	17	18	51
Occasional Abdominal Cramp	1	1	2	3	0	0	-	-
Occasional Digestive Disturbance	1	1	8	12	10	24	4	12
Occasional Neuritic Symptoms	0	0	5	7	2	5	-	-
Poor General Health	2	3	3	4	0	0	1	3

KC 01467

TABLE 20

Distribution According to Certain Objective Abnormalities of Groups of Subjects Not Exposed to Ethyl Gasoline - Examined in 1927

Type of Abnormality	71 Medical Students		69 Filling Station Attendants		42 Tank Wagon Handlers		35 Garage Mechanics	
	Number	%	Number	%	Number	%	Number	%
Under-nutrition	7	10	13	19	0	0	0	0
Pallor	1	1	3	4	0	0	0	0
Irritation of Skin of Hands	0	0	2	3	0	0	4	11
Lead Line	0	0	0	0	4	10	3	9
Tremors	2	3	9	13	0	0	0	0
Sensory Disturbances	3	4	9	13	2	5	1	3
Urinary Acidity	7	10	3	4	16	38	8	23
Albuminuria	1	1	3	4	3	7	3	9

LE 01468

TABLE 21

Distribution According to Systolic Blood Pressure of Groups of Subjects Not Exposed to Ethyl Gasoline, Examined in 1927

Blood Pressure Readings	Medical Students		Filling Station Attendants and Tank Wagon Handlers		Garage Mechanics	
	Number	%	Number	%	Number	%
100-109	1	1	2	2	0	0
110-119	22	31	15	13	6	17
120-129	23	33	32	28	14	40
130-139	17	24	29	25	7	20
140-149	7	10	15	13	5	14
150-159	1	1	9	7	3	9
160-169	0	0	2	2	0	0
170-179	0	0	1	1	0	0
180-189	0	0	1	1	0	0
190-199	0	0	3	3	0	0
200-209	0	0	3	3	0	0
210-219	0	0	1	1	0	0
220-229	0	0	0	0	0	0
230-239	0	0	1	1	0	0
Total	71	100	114	100	35	100

Mean	125.9	138.2	129.8
Probable Error of Mean	± 0.8	± 1.5	± 1.3
Standard Deviation	10.20	23.45	10.98

01469

TABLE 27

Distribution According to Haemoglobin of Blood of Groups of Subjects Not Exposed to Ethyl Gasoline, Examined in 1927

Haemoglobinometer Reading (Dare)	Medical Students		Filling Station Attendants and Tank Wagon Handlers		Garage Mechanics	
	Number	%	Number	%	Number	%
60-64	1	1	0	0	0	0
65-69	1	1	1	1	0	0
70-74	0	0	9	8	1	3
75-79	3	4	12	11	2	6
80-84	10	15	17	16	6	18
85-89	21	30	43	40	12	35
90-94	17	25	15	14	10	29
95-99	11	16	9	8	3	9
100-104	5	7	2	2	0	0
105-109	1	1	0	0	0	0
Total	70	100	108	100	34	100
Mean	89.8		86.0		89.0	
Probable Error Of Mean	±0.6		±0.5		±0.7	
Standard Deviation	7.78		7.15		5.73	

KG 01470

TABLE 2 [illegible]

Distribution According to Lead Found in Faeces of Groups of Subjects Not Exposed to Ethyl Gasoline, Examined in 1927

Milligrams of Lead Per Sample of Faeces	Medical Students		Filling Station Attendants		Garage Mechanics	
	Number	%	Number	%	Number	%
0 - 0.079	17	25	14	20	5	19
0.08 - 0.159	15	22	14	20	7	27
0.16 - 0.239	19	27	18	25	2	8
0.24 - 0.319	6	9	7	10	2	8
0.32 - 0.399	3	5	7	10	3	11
0.40 - 0.479	2	3	6	8	2	8
0.48 - 0.559	2	3	1	1	1	4
0.56 - 0.639	1	1	0	0	0	0
0.64 - 0.719	1	1	1	1	0	0
0.72 - 0.799	0	0	0	0	0	0
0.80 - 0.879	1	1	1	1	0	0
0.88 - 0.959	1	1	0	0	1	4
0.96 - 1.039	0	0	0	0	0	0
1.04 - 1.119	1	1	0	0	0	0
1.12 - 1.199	1	1	0	0	0	0
1.20 +	0	0.0	3*	4	3*	11
Total	70	100	72	100	26	100
Mean	0.232		0.197		0.235	
Probable Error of Mean	± 0.019		±0.013		± 0.029	
Standard Deviation	± 0.0236		±0.159		± 0.205	

*Excluded in calculation of means.

KE 01472

TABLE

Distribution According to Milligrams of Lead per Gram Ash of Faeces Of Groups of Subjects Not Exposed to Ethyl Gasoline, Examined in 1927

Milligrams of Lead Per Gram of Ash	Medical Students		Filling Station Attendants		Garage Mechanics	
	Number	%	Number	%	Number	%
0 - 0.049	29	48	29	41	12	46
0.05 - 0.099	16	27	26	31	6	23
0.10 - 0.149	9	15	8	11	1	4
0.15 - 0.199	3	5	4	6	2	8
0.20 - 0.249	1	2	0	0	1	4
0.25 - 0.299	0	0	1	1	1	4
0.30 - 0.349	0	0	1	1	1	4
0.35 - 0.399	0	0	0	0	0	0
0.40 - 0.449	1	2	1	1	0	0
0.55 - 0.599	1	2	0	0	0	0
0.65 - 0.699	0	0	0	0	2	8
1.50 - +	0	0	2**	2	0	0
Total	60	100	71	100	26	100
Mean	0.079*		0.077**		0.085 ⊕ 0.131	
Probable Error of Mean	±0.008		± 0.006		± 0.012 ⊕ ± 0.023	
Standard Deviation	0.094		0.071		0.085 ⊕ 0.177	

* Mean Calculated on a wider grouping of Findings
** Excluded in Calculation of Mean
⊕ Calculated after exclusion of two results over 0.65 milligrams

KE 01473

TABLE 26

Distribution According to Milligrams of Lead Per Liter of Urine of Groups Of Subjects Not Exposed to Ethyl Gasoline, Examined in 1927

Milligrams of Lead Per Liter of Urine	Medical Students		Filling Station Attendants		Garage Mechanics	
	Number	%	Number	%	Number	%
0.- 0.029	11	17	11	15	8	31
0.03 - 0.059	22	34	20	28	4	15
0.06 - 0.089	16	25	17	24	5	19
0.09 - 0.119	10	15	6	8	2	8
0.12 - 0.149	1	1+	4	6	5	19
0.15 - 0.179	1	1+	3	4	0	0
0.18 - 0.209	1	1+	5	7	0	0
0.21 - 0.239	1	1+	0	0	0	0
0.24 - 0.269	0	0	0	0	1	4
0.27 - 0.299	1	1+	0	0	0	0
0.45 - 0.479	0	0	1	1+	0	0
0.54 - 0.569	0	0	1*	1+	0	0
0.66 - 0.689	1*	1+	1*	1+	0	0
1.00 - +	0	0	3*	4	1*	4
Total	65	100	72	100	26	100

Mean	0.078	0.081	0.077
robable Error of ean	± 0.007	±0.006	±0.008
tandard Deviation	0.089	0.069	0.059

*Excluded in calculation of means

KE 01474

XIII and XIV, in Chapter III, only in that those who have had some degree of previous occupational lead exposure are included. For the second group, filling station attendants and bulk handlers of ordinary gasoline are ~~lumped together~~ 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 cooperate in the collection of samples. 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 Ethyl 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 objectively. 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 27 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 fact must be made from the tables of distribution.) Comparison of the means ~~shows~~ reveals a striking lack of statistical differentiation of the groups. The medical students show a significant difference in age, but in no other factor. The barrel fillers not exposed to Ethyl Gasoline show a significantly low haemoglobin content of their blood, as previously pointed out. The

TABLE 27

Summary of Mean Values of Age, Systolic Blood Pressure, Haemoglobin, and Excretion of Lead In Faeces and Urine, for Various Groups of Subjects.

Description of Subjects.	Age In Years	Systolic Blood Pressure (Sitting)	Haemoglobin Readings	Lead in Mgs. In Single Sample of Faeces	Lead in Mgs. Per Gram Ash In Faeces	Lead in Mgs. Per Liter of Urine	Number of Subjects
Medical Students Not Exposed to Ethyl Gasoline Examined in 1927	22.3 ±0.2	125.9 ±0.8	89.8 ±0.6	0.232 ±0.019	0.079 ±0.008	0.078 ±0.007	71
Filling Station and Tank Wagon Handlers not Exposed to Ethyl Gasoline-Examined in 1927	37.5 ±0.8	138.2 ±1.5	86.0 ±0.5	0.197 0.013	0.077 ±0.006	0.081 ± 0.006	114
Filling Station Attendants Exposed to Ethyl Gasoline Examined in 1929	40.8 ±1.2	130.1 1.7	80.9 0.67	0.258 ±0.018	0.087 0.007	0.071 ± 0.005	56
Tank Wagon Handlers Exposed to Ethyl Gasoline, Examined in 1929.	38.6 ±1.1	130.4 ±1.9	85.0 ±0.59	0.360 ± 0.023	0.120 ± 0.014	0.089 ± 0.011	50
Garage Mechanics Not Exposed to Ethyl Gasoline Examined in 1927	31.12 ±0.8	129.8 ±1.3	88.0 ± 0.7	0.235 ± 0.029	0.131 ± 0.023	0.077 ± 0.008	35
Garage Mechanics Exposed to Ethyl Gasoline, Examined in 1929	34.3 ± 0.5	125.7 ±0.7	84.5 ± 0.24	0.379 ± 0.012	0.131 ± 0.005	0.086 ± 0.004	201
Barrel Fillers Not Exposed to Ethyl Gasoline	37.9 ± 1.2	134.3 ±1.8	71.1 ± 0.92	0.380 ± 0.037	0.137 ± 0.014	0.058 ± 0.009	27
Barrel Fillers Exposed to Ethyl Gasoline	39.1 ±1.3	129.1 ± 2.3	83.3 ± 0.91	0.283 ± 0.[illegible]	0.113 ± 0.007	0.052 ± 0.004	22

KE 01476

mean lead content per sample of faeces shows certain statistically significant variations within the groups, but no actual significance can be attributed to these differences in view of the variability in the size of the faecal samples. When the latter factor is corrected by expressing the lead in the faeces in relation to the quantity of ash, the variability of the groups becomes statistically insignificant.

It has been intimated previously 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 leaded gasoline and its deposits on motor parts and elsewhere, might be expected to have some influence upon the lead absorption of the garage mechanic. As a means of ascertaining the significance 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 7 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. Considering the rate at which large quantities of lead have been shown to be eliminated from the body, the effects of previous slight or moderate exposure to lead, would not be expected to show themselves in an increased excretion after the lapse of years. Nevertheless it is of some interest and importance to establish the facts in the matter.

KE ■ 01477

TABLE

Mean Values of Lead in Faeces and Urine of Filling Station Attendants and Tank Wagon Handlers, Exposed to Ethyl Gasoline, Excluding All Results Obtained on Persons With Other Industrial Exposure to Lead Compounds.

	Filling Station Attendants Exposed to Ethyl Gasoline	Tank Wagon Handlers Exposed to Ethyl Gasoline	Combined Filling Station Attendants and Tank Wagon Handlers
Lead in Milligrams In Single Sample of Faeces	0.338 ± 0.043	0.277 ± 0.035	0.336 ± 0.030
Lead in Milligrams Per Gram Ash in Faeces	0.069 ± 0.009	0.116 ± 0.024	0.086 ± 0.011
Lead in Milligrams Per Liter of Urine	0.063 ± 0.009	0.063 ± 0.010	0.065 ± 0.007
Number of Subjects	19	15	34

It would appear that an examination into the relationship between length of service and lead excretion, might ~~give~~ a means of ascertaining the significance of the lead exposure associated with the occupation of the garage mechanics. This was done first by studying the correlation between the period of continuous employment as mechanics and lead excretion, and then by a corresponding study of the length of exposure in repairing cars which used Ethyl Gasoline, as against lead excretion. 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 of 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 Ethyl Gasoline. Among the subjects studied in 1929, there were twenty-six filling station attendants, and twenty-four tank wagon handlers who had been employed as subjects in 1927. Presumably, if their occupation contains a significant lead hazard-they should show some evidence of change in lead excretion after two years. The findings for the two years, as regards lead excretion, are shown in Tables 30, 31, and 32. The mean values are summarized in Table 33. It may be seen that no statistically valid difference is demonstrable.

TABLE 29

Showing Lack of Correlation Between Duration of Employment of Garage Mechanics and Lead Excretion, and Duration of Exposure to Ethyl Gasoline and Lead Excretion.

Factors Correlated	Correlation Coefficient
Length of Continuous Service as Garage Mechanic with Lead in Faeces in Milligrams per Gram of Ash.	+0.017 ± 0.056
Length of Continuous Service as Garage Mechanic with Lead in Urine in Milligrams per Liter	+0.023 ± 0.055
Length of Exposure to Ethyl Gasoline as Garage Mechanic With Lead in Faeces in Milligrams per Gram of Ash	+0.223 ± 0.099
Length of Exposure to Ethyl Gasoline as Garage Mechanic With Lead in Urine in Milligrams per Liter	−0.243 ± 0.099

KE 01480

TABLE 30

Distribution of Identical Subjects For the Years 1927 and 1929 According to Milligrams of Lead Found in Faeces.

Milligrams of Lead Per Sample of Faeces	Filling Station Attendants Exposed to Ethyl Gasoline				Tank Wagon Handlers Exposed to Ethyl Gasoline			
	1927		1929		1927		1929	
	Number	%	Number	%	Number	%	Number	
0 - 0.079	1	5	3	15	0	0	2	
0.08 - 0.159	6	30	3	15	3	17+	2	
0.16 - 0.239	2	10	8	40	4	23+	3	
0.24 - 0.319	3	15	0	0	3	17+	3	
0.32 - 0.399	2	10	3	15	2	12	1	
0.40 - 0.479	1	5	1	5	3	17+	3	
0.48 - 0.559	0	0	1	5	0	0	1	
0.56 - 0.639	2	10	1	5	2	12	1	
0.64 - 0.719	1	5	0	0	0	0	0	
0.72 - 0.799	0	0	0	0	0	0	0	
0.80 - 0.879	0	0	0	0	0	0	0	
0.88 - 0.959	0	0	0	0	0	0	0	
0.96 - 1.039	0	0	0	0	0	0	1**	
1.83	1*	5	0	0	0	0	0	
5.10	1*	5	0	0	0	0	0	
Total	20	100	20	100	17	100	17	

Mean	0.280	0.236	0.308	0.402*
Probable Error of Mean	±0.030	±0.023	±0.025	±0.036
Standard Deviation	0.187	0.153	0.150	0.218

* Excluded in calculation of mean.

** With exclusion of single high result, the mean becomes 0.365 ± 0.028

NOE 01481

TABLE 3

Distribution of Identical Subjects for the Years 1927 and 1929 According to Milligrams of Lead Per Gram Ash in the Faeces

Milligrams of Lead Per Gram of Ash	Filling Station Attendants Exposed to Ethyl Gasoline				Tank Wagon Handlers Exposed to Ethyl Gasoline			
	1927		1929		1927		1929	
	Number	%	Number	%	Number	%	Number	%
0 - 0.039	2	10	1	5	1	6	7	41
0.04 - 0.079	5	25	7	35	4	23+	2	12
0.08 - 0.119	5	25	6	30	5	30	3	17
0.12 - 0.159	3	15	3	15	4	23+	2	12
0.16 - 0.199	1	5	1	5	3	17	1	6
0.20 - 0.239	0	0	1	5	0	0	1	6
0.24 - 0.279	1	5	1	5	0	0	0	0
0.28 - 0.319	0	0	0	0	0	0	0	0
0.32 - 0.359	0	0	0	0	0	0	0	0
0.36 - 0.399	0	0	0	0	0	0	0	0
0.40 - 0.439	1	5	0	0	0	0	0	0
0.44 - 0.479	0	0	0	0	0	0	0	0
0.57	0	0	0	0	0	0	1**	6
0.64	1*	5	0	0	0	0	0	0
1.36	1*	5	0	0	0	0	0	0
Total	20	100	20	100	17	100	17	100

Mean	0.118	0.106	0.109	0.142 **
Probable Error of Mean	± 0.015	± 0.009	±0.008	±0.019
Standard Deviation	0.093	0.058	0.047	0.117

*Excluded in calculation of mean

** With exclusion of single high result the mean becomes 0.118 ± 0.010

WEB 01482

TABLE 32

Distribution of Identical Subjects for the Years 1927 and 1929
According to Milligrams of Lead Per Liter of Urine

Milligrams of Lead Per Liter of Urine	Filling Station Attendants Exposed to Ethyl Gasoline				Tank Wagon Handlers Exposed to Ethyl Gasoline			
	1927		1929		1927		1929	
	Number	%	Number	%	Number	%	Number	%
0 - 0.039	3	11	7	27-	0	0	6	25
0.04 - 0.079	9	35	7	27-	10	42	11	46
0.08 - 0.119	6	23	9	35	5	21	2	8+
0.12 - 0.159	3	11	0	0	3	11+	1	4+
0.16 - 0.199	1	4	1	4	1	4+	1	4+
0.20 - 0.239	2	8	1	4	0	0	0	0
0.24 - 0.279	0	0	0	0	0	0	1	4+
0.28 - 0.319	0	0	0	0	0	0	0	0
0.32 - 0.359	0	0	0	0	1	4+	1	4+
0.36 - 0.399	0	0	0	0	1	4+	0	0
0.40 - 0.439	0	0	0	0	1	4+	0	0
0.58	1	4	0	0	0	0	0	0
0.87	1	4	0	0	0	0	1	4+
1.00	0	0	1	4	0	0	0	0
4.00 - +	0	0	0	0	2*	8+	0	0
Total	26	100	26	100	24	100	24	100
Mean	0.142		0.111		0.129		0.115 **	
robable Error of ean	± 0.024		±0.025		±0.015		±0.024	
tandard Deviation	0.180		0.188		0.106		0.173	

* Excluded in calculation of mean
** Mean drops to 0.083 ± 0.11 when one result of 0.87 milligrams is excluded.

VE 01483

TABLE 33

Summary of Mean Values of Lead Found in Samples of Faeces, of Lead in Milligrams per Gram of Ash in Faeces, and of Lead in Milligrams Per Liter of Urine for Identical Subjects Examined in 1927 and 1929.

	Filling Station Attendants Exposed to Ethyl Gasoline		Tank Wagon Handlers Exposed to Ethyl Gasoline		Combined Filling Station Attendants and Tank Wagon Handlers	
	1927	1929	1927	1929	1927	1929
ead in Milligrams in ingle Sample of Faeces	0.280 ± 0.030	0.236 ±0.023	0.308 ±0.025	0.402 ±0.036	0.294 ±0.019	0.312 ±0.022
ead in Milligrams Per ram Ash in Faeces	0.118 ± 0.015	0.106 ±0.009	0,109 ±0.008	0.142 ±0.019	0.114 ±0.008	0.124 ±0.011
ead in Milligrams Per iter of Urine	0.142 ± 0.024	0.111 ±0.025	0.129 ±0.015	0.115 ±0.024	0.136 ±0.015	0.113 ±0.017
umber of Subjects	26	26	24	24	50	50

KE 01484

Chapter VII

Certain Considerations in the Prevention, Diagnosis and Treatment of Lead Poisoning

1. The Prevention of Lead Poisoning Among the General Population.

The necessity for further detailed knowledge of the opportunities for lead absorption under present conditions, and the anticipation of new opportunities arising from changes in the life and activities of the community.

At present the largest factors which differentiate the modern community from primitive life are found in candies and fruits. The spraying of fruits and leafy green materials with lead arsenate is the largest of these factors.

Necessity for particular caution in the lead contacts of young children (cite literature) because of their apparent susceptibility, their unusual behavior - pica and their natural tendency to have hands and other objects in their mouths - and the disproportionate frequency of encephalitis. Inexperienced and ignorant manufacturers of beds, toys, etc. coated with lead paint. Repainting by parents or others. Drinking water, lead nipple shields, lead-containing cosmetics on mother's skin. Other items of importance. Typical case records

2. The Prevention of Lead Poisoning in Industry.

The recognition of exposure to lead compounds - air sampling methods versus studies of lead excretion. (See typed article on this subject.)

The limitation of exposure - means to be suited to occasion. Sharp segregation coupled with measurements of exposure as influenced by improved methods of eliminating danger. Not adequate until lead poisoning is completely eliminated. This means exposure must not be sufficient to injure even susceptible persons. Careful medical

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supervision will usually serve to prevent tragedies while the methods are being perfected: Rejection of diseased persons in lead trades. Symptoms and signs of impending intoxication. Stippling and other blood changes.

What are safe limits of industrial lead exposure in terms of the methods of measuring exposure? For practical purposes the exposure must be reduced at least to the point where the lead excretion of representative groups of workers is within the limits which are not associated with the occurrence of lead poisoning. It should be limited to such even lower levels as are compatible with the application of reasonable methods of control. If this can not be done except at an expense which brings economic ruin to a lead industry, it would seem that society could better endure the loss of the industry than to pay the price exacted by its continuation.

3. The Diagnosis of Lead Poisoning.

Three points: 1. History of exposure. 2. Characteristic symptoms and signs. 3. Establishment of significance of exposure - knowledge of conditions and their relation to cases of lead poisoning. Chemical analysis in appraisal of exposure.

Difficulties in case of sequelae - malingering, vague subjective symptoms, non-specificity of symptoms or signs or sequelae.

There is no laboratory short-cut to a diagnosis. The only thing the laboratory can do at present is to establish the significance of the exposure.

Studies of faecal excretion within twenty-four hours of cessation of exposure give magnitude of exposure in dusty trades.

Studies of urinary excretion of more value under the usual conditions because of the persistence of abnormal findings, uncomplicated to a large extent, by dietary lead.

The laboratory signs of lead intoxication - valuable but not specific or final. Lead in excreta, lead in blood, blood changes.

Typical cases: Observations following immediately after exposure. Delayed observations.

The curve of lead elimination in urine - Smith, Foster, Jones. The slope of the curve in relation to severity of exposure. With knowledge of the time interval since exposure, and with two or more points established the curve in any instance can be projected to give a measure of the relative magnitude of the exposure.

Fatal cases without observations prior to death.

Post mortem analyses and their significance.

Concentration of lead in certain tissues as liver and blood.

Gross amount of lead as indicative of significant exposure.

The time of exposure may be determined with some degree of accuracy from the quantity of lead present. The extent of the exposure can be determined if the time factor (since exposure) is known.

The accumulation of information as to the amounts of lead present in human tissues in relation to determined rates of lead excretion may eventually facilitate the formation of accurate estimates in terms of actual amounts of lead in the body. If this be accomplished analytical methods alone will serve to answer some of the questions which present themselves at the necropsy table. The amounts of lead in the tissues of an individual who has died under conditions which permit suspicion of the existence of significant lead exposure will then establish the facts, in relation to the time interval between cessation of exposure and death.

Typical cases: (1) normal amounts of lead. (2) abnormal amounts of lead.

Lead in the brain and its significance. Typical cases: no exposure; significant exposure.

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4. The Treatment of Lead Poisoning.

Removal from exposure.

Normal elimination of lead versus induced elimination. (1) Unnecessary. (2) Dangerous, especially in children and severely exposed. (3) Unavailing because of brevity even if doubtful accuracy of observations be ignored, and because of the brevity of periods of treatment. Such brevity enforced by reason of economic necessity. Hospitalization and medical care are costly and are not provided for by compensation courts.

Rest, freedom from anxiety including economic.

Full diet, profuse liquids, alimentary tract kept freely eliminating. $MgSO_4$, etc.

5. Compensation Cases of Lead Poisoning.

Proof of exposure in relation to occupation.

Duration of disability.

Re-employment.

6. Theoretical Considerations.

In view of the conservatism of the conclusions which have hitherto been drawn from the data which have been presented the writer may be permitted to indulge in a few speculations as to the meaning of certain matters which have had only a partial or practical interpretation. Perhaps such efforts may bring into relief some of the problems which require solution.

See typewritten article on subject.

The factors which are active in the production of lead poisoning are but poorly understood. Why is it that one individual may be exposed to a certain set of conditions for years without apparent injury, while another becomes ill after a short period of exposure? Or why does one and the same individual persist in good health for a long time only to develop an unanticipated acute attack of colic or

neuritis or encephalitis. One may suspect that in many instances these results have arisen because of the presence of diseased persons in lead trades, or because the signs of impending intoxication were not sought for. Certainly the term "unusual susceptibility", has been a most convenient term under which to conceal faulty observations, and by means of which to sidestep the responsibility for the maintenance of unnecessarily hazardous conditions in lead trades. Nevertheless, variability in susceptibility is a fact which must be dealt with in the interpretation of the nature of lead poisoning. Does lead accumulate in the tissues of some individuals to a greater extent than in others, and does this occur more readily under certain physiological conditions than under others in the same person? If so there must be a certain variability in the chemical compounds of lead in the body under a variety of conditions. The nature of these compounds and their reactivity under various conditions, must be known before we can hope to understand the mechanisms of lead absorption and lead intoxication.

Some clue to the existence of important chemical compounds in the body may be found in the relationship which apparently exists between the rate of lead absorption and the rate of urinary lead excretion. (Plot accurate curve of faecal lead content (exposure) versus urinary lead concentration, showing the point at which a critical break occurs.) At a certain point in the absorption, elimination fails to keep pace, showing little or no proportional relationship to absorption. At this point the excretory ability of the kidneys reaches a maximum or else some chemical reaction has reached its limit, thus permitting the lead to be distributed into the tissues. Something definitely modifies the release of lead from the body. This point is probably the beginning of rapid accumulation of lead, and if it can be established definitely in relation to exposure it should be easily possible to distinguish between a safe level of lead exposure, and

that is not safe. At this point any individual is in danger of being poisoned. Presumably susceptible persons reach this point in advance of normal individuals, as an expression of the existence of chemical factors which promote accumulation, or conversely, as a consequence of the absence of chemical factors which promote elimination. That this is not always a matter of disease, but may occur within the limits of normal physiological states is demonstrated by the susceptibility of infants and children.

~~Chapter II~~

Appendix

Experimental Methods.

In a field as many-sided and as replete with possibilities of error as the one under discussion, ~~it is obvious that~~ the validity of experimental results or conclusions depends primarily upon the accuracy and adequacy of methods of procedure. In fact, one of the ~~greatest~~ obstacles to a proper interpretation of much of the ~~previous~~ work on lead compounds arises from the fact that methods are not described with sufficient definiteness to justify judgments as to their accuracy or to permit of their duplication. Therefore at the risk of introducing intrinsically tedious material, ~~it becomes necessary to set down details of~~ experimental methods are given in detail in the following paragraphs.

1. Analytical Methods

(1) Analysis of Urine.

Samples of urine are collected in gallon jugs of the type used for fruit juices. The volume is measured and for every liter of urine 100 c.c. HNO_3 (Sp.Gr. 1.42) and 10 c.c. H_2SO_4 (1:10) are added, with ~~considerable~~ care when dealing with ammoniacal samples. (H_2SO_4 is used to avoid excessive alkalinity of the ash.) The sample is evaporated to dryness on a hot plate at approximately 105° C., is transferred to a 500 c.c. Pyrex dish and again evaporated to dryness at 105° C. After ashing in an electrical muffle furnace at a temperature controlled by pyrometer so as not to exceed

500° C., the material is cooled, moistened ~~carefully~~ cautiously with distilled water, and treated with 20 c.c. HNO_3 (1:1), the ash being broken up with a stirring rod. Distilled water is added to bring the volume to 50 c.c. and, following digestion on a hot plate, the residue is filtered off and discarded after repeated washing, alternately, with hot HNO_3 (1:1) and hot water, the filtrate and washings being caught in a 600 c.c. Pyrex beaker. The filtrate is evaporated to dryness on a hot plate at 105° C. The residue is treated with [redacted] 25 c.c. conc. HCl. and again evaporated to dryness. The residue is dissolved in HCl (1:1), is diluted to 300 c.c. and is neutralized by adding 25% NaOH until just alkaline, 4 drops of 0.1% aqueous methyl orange serving as indicator. HCl (1:2) is added to the faintest pink, the solution is cooled, and gassed with H_2S for one hour. After standing overnight the precipitate is filtered off on a 12.5 cm. Whatman #40 filter paper and is washed thoroughly with freshly prepared H_2S water to which has been added 0.1% of its volume of HCl. The precipitate is washed off the paper into the beaker in which it was produced, by means of hot HNO_3 (1:1), followed by hot water, the sides of the beaker and the gassing tube being similarly washed. The solution is evaporated to small volume, transferred to a 100 c.c. Pyrex beaker, treated with 1 c.c. H_2SO_4 (Sp.Gr. 1.84) and evaporated to fumes of H_2SO_4.* After cooling ~~it is taken up in~~ 30 c.c. of a mixture of 10 c.c. 95% ethyl alcohol and 20 c.c. water are added, the solution allowed to stand over night. The precipitate is collected on a 7 cm. Munktell #1-F filter paper, thoroughly washing the beaker and

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* After cooling, the sides of the beaker are washed with distilled water and the solution again evaporated to fumes of H_2SO_4. (This treatment is necessary to destroy nitrosyl-sulphuric acid during the first fuming.)

paper with a solution containing 1 c.c. H_2SO_4 (Sp.Gr. 1.84) to 10 c.c. 95% ethyl alcohol and 20 c.c. water. It is then dissolved off the paper into a 600 c.c. Pyrex beaker with [redacted] hot 20% ammonium acetate, followed by hot water. (This is [redacted] done by first washing the sides of the beaker in which the precipitate was made with 5 c.c. of the ammonium acetate solution, then decanting the solution and washings through the filter.) This solution, now diluted to 300 c.c. with cold water, is treated with 2 drops HNO_3 (Sp.Gr. 1.42), and is neutralized by adding 25% NaOH to alkalinity, then HCl (1:2) to a faint pink to Methyl Red (4 drops of a 0.1% solution of Methyl Red in 50% ethyl alcohol). 1 c.c. HCl (1:2) is added in excess, the solution is cooled, gassed for one hour with H_2S and allowed to stand overnight. The precipitate is filtered off, washed and redissolved by the same methods and precautions as employed at the previous sulphide step. The solution is evaporated to 1 or 2 c.c., and transferred to a 150 c.c. Pyrex beaker, where it is diluted to 80 c.c. with cold water, neutralized with 25% NaOH (free from iron and aluminium), with 4 drops of a solution of 0.5% phenolphthalein in 1% aqueous NaOH, as indicator. 5 drops of 25% NaOH are added in excess, for the purpose of supplying enough sodium acetate to repress the H^+ ion concentration due to the presence of small amounts of mineral acids, when the solution is neutralized with 5% acetic acid. After adding 2 c.c. of 5% acetic acid in excess of that required for neutralization, the solution is brought to a boil and treated with 2 c.c. of 1% K_2CrO_4 solution, the mixture standing on a hot plate for one hour, and at not

less than 60°C. overnight. The precipitate is collected on a 7 cm. Munktell #1-F paper, the beaker and paper being washed ~~with cold~~ thoroughly with hot water to remove the last traces of soluble chromate (tested with diphenyl carbazide till washings do not give a pink coloration), and is then dissolved into a 250 c.c. Mohr flask containing 100 c.c. water, by means of ~~25~~ 50 c.c. cold HCl (1:5) followed immediately by cold water. The beaker and stirring rod are washed and the washings are decanted through the paper. In a similar flask a standard is prepared containing sufficient $K_2Cr_2O_7$ solution to be equivalent to 0.30 mgs. lead, precipitated as $PbCrO_4$. 100 c.c. water and ~~25~~ 50 c.c. cold HCl (1:5) are added. To the sample and to the standard, 2 c.c. of a 1% solution of S-diphenyl carbazide in glacial acetic acid are added. After the dilution of each to 250 c.c. and after thorough mixing, the estimation of lead in the sample is accomplished by comparing the intensity of the pink color with that of the standard, with a Duboscq colorimeter.

* Note: If the sulphide separation becomes too unwieldy a coagulating precipitate or fine colloid is obtained it is best to carry out a duplicate separation as described above.

(2) Analysis of Faeces

Samples of faeces are collected in glass-capped quart or pint preserve jars. Each sample is transferred to a 500 c.c. weighed silica dish, dried to constant weight on a hot plate at 105° C., and then ashed in the same dish in an electrical muffle furnace at a temperature controlled by pyrometer so as not to exceed 500° C. After cooling and weighing the ash, distilled water is added ~~with care~~ carefully and the moistened ash 1 or 2 c.c. nitric acid solution of the sulphide is evaporated to dryness to eliminate hydrogen sulphide and to reduce

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ash is treated with 20 c.c. HNO_3 (1:1) while being broken up with a stirring rod. Hot water is added to bring the volume to 50 c.c. A period of digestion on a hot plate is followed by filtration into a 600 c.c. beaker, the residue being thoroughly washed alternately with hot HNO_3 (1:1) and hot water, and discarded. The combined filtrate and washings are evaporated to dryness on a hot plate. The residue is The residue is treated with 25 c.c. Con and a gas evaporate to dry dissolved in HCl (1:1), is diluted to approximately 300 c.c. in a 600 c.c. beaker, and is neutralized with 25% NaOH, added drop by drop with constant stirring until a slight permanent turbidity is present. The solution should be cool, and should not be permitted to become appreciably warm while being neutralized. A few drops of 0.5% aqueous solution of methyl orange are added, and if the solution is alkaline HCl (1;2) is added to a faint pink. Following treatment with H_2S for one hour the precipitate is allowed to settle overnight and is filtered on a 12.5 cm. Whatman #40 filter paper and is washed with freshly prepared H_2S water to which has been added 0.1% of its volume of HCl. It is then re-dissolved into the beaker in which the sulphide precipitation was made, by means of hot HCl (1:1), to which has been added 10 drops of concentrated HNO_3, in order to dissolve any CuS and thereby prevent occlusion of lead. The sides of the beaker and the gassing tube are washed down with the acid, and the paper is further washed well with hot water. The solution is permitted to digest until all the H_2S has been driven off, whereupon it is diluted with cold water to 300 c.c. From this point on, the second neutralization with NaOH, the second precipitation with H_2S, and the

subsequent steps of the analysis proceed exactly as in the case of the urinary sample.

(3) Analysis of Food, Tissues and Other Materials.

These materials are collected in glass-capped quart mason jars. Except for those which contain large amounts of calcium or fat, the general procedure, after weighing, is to introduce suitable quantities into 600 c.c. Pyrex beakers together with 10 to 20 c.c. concentrated HNO_3, 7 c.c. concentrated HCl, and 5 to 10 c.c. concentrated H_2SO_4, taking down to a char on a hot plate. The char is destroyed by frequent additions of small amounts of concentrated HNO_3. Near the end of the process 2 c.c. 60% perchloric acid are added, while additional amounts of HNO_3 are introduced until no char appears on evaporation to H_2SO_4 fumes. The material is evaporated to small volume, cooled, and treated with 10 c.c. concentrated HCl and 350 to 400 c.c. water. The regular analysis is carried on from this point.

No H_2SO_4 is used in the digestion of bone or of tissues which contain bone. Such materials are treated with sufficient HNO_3 (1:3) to complete digestion, after which the sample is evaporated to dryness on a hot plate at approximately 110° C. The residue is taken up in 50 c.c. concentrated HNO_3 and hot water, transferred to a silica dish, again evaporated to dryness, and ignited to a white ash in the electric muffle furnace at a temperature not higher than 500° C. The ash is moistened carefully with water, is treated with 50 c.c. concentrated HNO_3,

and set on a hot plate until dissolved. The residue is filtered off and washed alternately with hot HNO_3 (1:1) and hot water. The filtrate is evaporated to dryness. The residue is dissolved in concentrated HCl, is again subjected to evaporation to dryness and is finally taken up in a minimal quantity of concentrated HCl (1:1). Upon being diluted with water to approximately 300 c.c., the usual analysis is carried out.

Fatty materials are dealt with most satisfactorily by heating with concentrated H_2SO_4 to an incipient char, after which they are treated with successive small portions of concentrated HNO_3 until no further char is present. The sulphuric acid solution is evaporated to small volume, whereupon the slight char which appears is destroyed with small amounts of concentrated HNO_3 and 60% perchloric acid. This entire procedure is accomplished with speed and convenience if the sample is divided into small quantities in Kjeldahl flasks. Constant attention is required.

(4) Remarks on Analytical Methods.

A survey of analytical methods in 1924, resulted in our use of those developed by Fairhall, with certain modifications instituted by [illegible] Edgar. Further efforts to shorten the method and to reduce the slight losses of lead to the minimum, resulted in investigation of technical procedures originating in the minds of the laboratory staff, or suggested by the work of Avery, Hemingway,

Anderson and Read[2], Taylor[3], Francis[4] and his associates, and Tannahill[5]. The preparation of [redacted] samples for analysis by primary ashing at low temperatures (500° C.), ~~has been~~ was abandoned in favor of initial wet digestion methods except in the case of faecal samples. Furthermore ~~it has~~ seemed safer not to place too great dependence upon the quantitative separation of lead from urine by treatment with ammonia as suggested, with certain qualifications, by Fairhall[6], or by precipitation with the oxalates as recommended by Taylor[3], though we have not investigated the latter method. The sulphate step, after the manner of Avery[2] et al., has been found ~~to be~~ [redacted] necessary to avoid the inclusion of materials other than lead. The colorimetric determination in which chromate ion is measured by means of S-diphenyl carbazide has been so satisfactory in our hands that we have been loathe to eliminate it in favor of a thiosulphate titration, sulphide precipitation, or the acid sulphite method of Ivanov[7]. The thiosulphate titration method ~~cannot be relied upon, is eliminated from consideration, in our judgment~~, in ~~dealing with~~ estimating amounts as low as a few hundredths of a milligram. The ~~fact that~~ dependence of the carbazide reaction ~~depends~~ upon chromate instead of lead becomes ~~of minor~~ an insignificant objection to its use when ~~considerations~~ it is recognized that the ~~complete~~ elimination of soluble chromate may be ~~satisfactorily~~ achieved ~~accomplished~~ by ~~the same~~ ~~[illegible]~~ care required ~~to avoid~~ in avoiding the inclusion of non-lead materials in ~~the~~ other two colorimetric reactions. An advantage in the use of S-diphenyl carbazide is found in the identical

quality of the colors produced in the standard and the sample, ~~a matter rarely accomplished in colorimetric~~ comparisons, ~~in~~ [redacted].

It would be highly desirable to dispense with the numerous steps of a purely chemical method, which involve slight but inevitable losses of lead. Nevertheless the results of our investigations derive their significance from the certainty that the methods have not yielded errors on the high side. Thus while slight uniform losses of lead are to be deplored, they do not influence the validity of the results, ~~which could not have been obtained with less sensitive methods, on the one hand, nor with more sensitive but less uniformly accurate procedures on the other.~~ Furthermore, certain definite advantages have accrued from the accumulation of comparable data over a period of years. ~~The gradual modification of methods on the basis of [redacted] ascertained~~ facts, while ~~maintaining technical uniformity otherwise, has~~ yielded a body of increasingly conclusive information.

~~3. Materials and Technique~~ 01499

Satisfactory results from the employment of any method of analysis for lead are predicated on the utmost care against the introduction of lead from containers, reagents, and experimental procedures. The opportunities for contamination in the laboratory are slight, ~~however~~, as compared to those associated with the collection of samples. ~~of any kind.~~ It is necessary to

supply chemically clean containers of glass which will not yield appreciable quantities of lead to the sample regardless of any chemical changes which may occur. It is essential to make sure that materials are collected into these containers, without the use of any intermediate vessel, and with adequate precautions against foreign materials which may be present in the air or upon the hands or clothing of subjects. Continual attention to these details is required to avoid gross contamination. Where intermediate containers are unavoidable as in case of persons confined to bed, special equipment is required which must be handled with laboratory technique. ~~The largest portion of~~ In the main our samples have been collected in glass-capped preserve jars, and in gallon jugs with cork stoppers. These have been cleaned in the laboratory with the same care as that employed in the case of the other glassware. The technique here is of some consequence. Tap water as well as cleaning reagents may contain appreciable quantities of lead. Special care is needed to assure lead-free distilled water. Thus the tap water and the distilled water are analyzed from time to time to assure their satisfactory quality, while the best quality of Sulphuric Acid and Sodium Dichromate is used as the cleaning solution, in order to avoid the contamination of lead found frequently ~~in considerable quantities~~ in the commercial ~~varieties~~ products. The possibilities of contamination from the glass containers have been tested by treating certain ones selected at random, with half their volume of hot nitric acid, allowing them to stand on a hot plate at 105° C. for two days,

after which the acid and washings were analyzed for lead. The highest results obtained have been 0.01 milligrams of lead, in the case of certain quart preserve jars. The gallon jugs have yielded no measurable quantity of lead under this treatment. To determine the maximal possibility of contamination certain of the containers have been broken. One-gram samples were decomposed with chemically pure sulphuric and hydrofluoric acids, and after fuming the residue to remove hydrofluoric acid analyses for lead were carried out. Mason jars are somewhat variable in their lead content, results varying from nil to 0.2 milligrams of lead per gram. The gallon jugs contain uniformly negligible amounts.

Corks used to stopper the bottles, and rubber rings used to seal the jars have been analyzed. A typical determination showed 0.07 milligrams of lead in 5.45 grams of rubber ring, while 6.6 grams of cork yielded no lead.

The glassware used in the analytical procedures contains measurable quantities of lead when decomposed with hydrofluoric acid and analyzed. However, the amount of glass actually dissolved is quite small, and in no way influences the results, as shown by blank determinations.

Lead-free reagents may be purchased, but considerable care must be taken to test them in this regard. Having established a source of satisfactory supply, a uniform purity is reasonably assured, but it is desirable to keep a continual check on the matter by making regular blank determinations. We have made a practice of running not less than two such control determinations with every set of analyses, thereby ~~securing~~ acquainting

ourselves ~~of~~ and the amounts of lead which may be contained in the maximal amounts of all the reagents employed in a single analysis, while at the same time testing the uniformity of the analytical procedures in the hands of the laboratory staff. Over a period of many months 96% of all such blanks have failed to show traces of lead. In no case has the quantity exceeded 0.02 milligrams of lead.

By means of scrupulous care in carrying out the technique of the analytical work, and by maintenance of the utmost cleanliness of the analytical laboratory, as well as a continual check on materials, equipment and technique, it has been possible to ~~provide a safeguard~~ against high results. Slight loss of lead is unavoidable, ~~because of the solubility of lead compounds which usually may be regarded as insoluble.~~ The results, therefore, err on the low side. The extent of such errors is indicated by a typical experiment designed to test the analytical procedures only, i.e. in the absence of organic materials.

Lead-free control samples containing 2.5 grams $CaCl_2$, 4 grams $Na_3PO_4.12H_2O$, 10 c.c. HCl (Sp. Gr. 1.19) in about 300 c.c. distilled water, were treated with variable quantities of lead unknown to the analytical staff. The results are shown in Table I.

Table I

Tests of the Sensitivity of Dithizone to Lead

Milligrams Lead Added	Milligrams Lead Found	Milligrams Lead Added	Milligrams Lead Found
Nil	Nil	0.20	0.14
Nil	Nil	0.20	0.14
Nil	Nil	0.20	0.12
Nil	Nil	0.20	0.15
0.07	0.05	0.25	0.18
0.07	0.04	0.25	0.18
0.07	0.04	0.25	0.16
0.07	0.04	0.25	0.19

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3. Methods of Estimating Basophilic Stippling of the Erythrocytes.

The recognized occurrence of changes in the character of the erythrocytes of the blood, in relation to the absorption of lead compounds, is of a specific importance to microscopic examinations of the blood in clinical or experimental work which concerns itself with lead. Without preconception as to the relative merit of the methods of detecting variations in the content or distribution of basophilic material in red blood corpuscles, we have elected to make observations on the occurrence of stippling in blood smears unmodified by fixation, haemolysis or by vital stains. The adoption of this as a general procedure on all cases, even where in some instances additional methods were employed, was based on the impossibility of sampling by any other means than that of a dried smear, under certain conditions of our work. Thus we have attempted to obtain a satisfactory degree of quantitative accuracy in a simple method applicable to any subject at any distance from laboratory facilities.

Several films are made from the blood of each subject, on chemically clean glass slides. Care is exercised to obtain uniformity of thickness and evenness in the distribution of erythrocytes as is possible, on chemically clean slides. The slides are permitted to dry naturally. They are labeled with the subject's name or number and the date, They may be examined in the laboratory at once or even weeks later and are kept clean and dry until they can be examined. (20 TP)

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~~without any demonstrable change, if they are kept dry and clean.~~ At ~~this time~~ they are inspected in the laboratory, and the best and most uniform ones are selected for staining. The stain employed is made up of 1.5 grams methylene blue, 0.2 c.c. of 1% NaOH in methyl Alcohol, in 100 c.c. methyl Alcohol. The smears are immersed in the stain for four seconds, washed rapidly with 0.025% aqueous $NaHCO_3$ solution, and dried ~~quickly~~ rapidly ~~preferably~~ in a strong air current.

The resultant stain is brilliant, and the stippled erythrocytes are easily recognized. The erythrocytes are stained a pale green, while the basophilic granules are a very dark blue. The criterion of the satisfactory quality of the stain is the relation existing between the pale green translucent appearance of the erythrocytes and the depth of the nuclear staining of the polymorphonuclear leucocytes.

~~Some little~~ Experience, careful technique, and microscope lenses capable of excellent definition are required to obtain good results. ~~It is desirable to examine~~ The smears are examined in a strong light, with a magnification of not less than 900 diameters. Every erythrocyte in each of fifty fields is scrutinized, since the count can be made more accurately by this means than by the examination of ~~Fifty fields are examined, by which is meant the~~ ~~every erythrocyte in the field. In our experience, such an~~ ~~examination is far more effective than is the observation of~~ the central portions of a great many more fields. Fields of identical area are obtained through the use of a standard microscopic equipment. ~~in observations in which the same microscopic equipment is employed.~~ The ~~Careful~~ selection of fields of most nearly uniform distribution of erythrocytes reduces the variation in the

number per field. ~~Nevertheless considerable variation in this factor occurs.~~ The number per field averages approximately 250, ~~in a series of observations.~~ so that ~~There~~ fifty fields ~~[illegible]~~ contain approximately 12,500 erythrocytes.

Reference, careful technique and the use of microscopes lenses which give sharp definition are ~~Some~~ appreciation of the limits of quantitative accuracy obtainable, in view of ~~[illegible]~~ the opportunities for variation in technique in the hands of a single careful worker, may be had from a consideration of the observations of Table II. Ten successive smears of the blood of each of three subjects were made, after which the microscopic examinations were carried out by one person.

Variations in the results obtained by two persons are shown in Table III. Each observer made ten successive counts on a single smear, thereby showing the limits of variation in the technique of microscopic examination. Then each observer made one smear from successive drops of the blood of the same subject and again made ten counts on the smear so prepared. The comparison of these two sets of results ~~gives some idea of~~ illustrate the variability which may arise from the preparation of smears, plus the microscopic technique.

~~It may be seen that there is a fair degree of accuracy in the procedure. In fact, a consideration of~~ The data which ~~[illegible]~~ appear in subsequent pages shows that the accuracy of observation is greater than the accuracy of interpretation in relation to the question at issue.

4. General Clinical Methods KE 01506

~~It is quite clear that~~ The excellence of clinical observations is dependent upon the skill, care, and judgment of the observer rather than upon specific methods. ~~Thus, it is scarcely profitable to describe procedures. It is of some importance, however, to point out the essential purposes~~ However reference must be made to the types of information which were sought, and to the chief purposes

Table II

Observations on Ten Successive Smears made from Same Subjects

Number of Stippled Erythrocytes found in 50 Fields

Smear	Subject B.	Subject J.	Subject N.S.
1	5	19	141
2	11	26	145
3	9	17	180
4	7	26	135
5	11	19	163
6	7	22	165
7	9	24	138
8	14	21	169
9	7	31	150
10	5	13	131
Average	8.5	21.8	151.7

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Table III

Observations on Successive Drops of the Blood of a Single Subject, as carried out by Two Persons, Each of whom has examined the Smear Made by Himself.

Observations on Single Smear

Observation	Stillial Erythrocytes Counted in Fifty Fields by D.	by S.
1	28	30
2	38	36
3	31	36
4	37	32
5	40	38
6	34	33
7	29	34
8	39	35
9	38	35
10	32	38
Average	35.6	34.7

Observations on Two Smears from Same Subject

Observation	Stillial Erythrocytes Counted in Fifty Fields by D.	by S.
1	135	89
2	110	91
3	141	110
4	119	101
5	117	97
6	118	106
7	115	92
8	117	85
9	113	110
10	113	106
	119.8	98.7

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of the clinical studies. Four general considerations influenced the selection of methods.

1. ~~Systematical~~ questioning of every subject was required, in order to determine the occurrence, duration and significance of this exposure to lead compounds. So many trades involve some contact with lead that ~~careful scrutiny of~~ the entire occupational history ~~must be made to determine this matter~~ had to be considered.

2. In studies which were concerned with normal processes ~~sure to lead compounds~~, it was desirable to ~~exclude~~ and to eliminate individuals who exhibited evidences of chronic or acute disease which might interfere with normal absorption, metabolism and excretion.

3. Where the factor of occupational lead exposure was under examination ~~effort was made to detect evidences of illness of any kind~~ special attention was given to the discovery of abnormalities associated with lead intoxication.

4 For the sake of ~~accurate~~ comparisons of various subjects or groups of subjects, information of a quantitative character was obtained so far as possible. ~~Statistical studies of such data, and of all other matters amenable to mathematical treatment, have been carried out as a regular procedure.~~

4. Information of a quantitative character was obtained so far as possible, in order to furnish data for statistical comparisons of various subjects and groups of subjects.

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