Statement to the Committee of Enquiry on Lead Ethyl Petrol
by
Graham Edgar, Ph.D.,

Director of Research
Ethyl Gasoline Corporation
New York City, USA.

(1) Introduction.

Before entering into technical matters the writer wishes to express to the Committee the desire of the Ethyl Gasoline Corporation to be of any assistance to the committee that may be possible. The Ethyl Gasoline Corporation has endeavored during its entire existence to determine as carefully and as completely as possible, the facts concerning all phases of the use of tetraethyl lead in motor spirit. The entire results of its own investigations, as well as all other results of which it is aware, have already been placed at the disposal of the Committee. The Corporation looks forward with great interest to the investigations of the Committee, and will welcome any new facts which these investigations may bring to light.

The Corporation desires to express to the Committee the assurance that any member of its technical personnel will be available to the Committee, should they so desire, particularly Dr. Robert A. Kehoe, Associate Professor of Physiology of the University of Cincinnati, who has carried out much of the medical research, and who will be glad to appear before the Committee at some later date should the Committee request it.

In the remainder of this report the writer desires to outline the history of the various medical investigations which have been carried out on petrol containing tetraethyl lead; to summarize briefly the more important conclusions which have been reached; and to give the

writer's personal interpretation of certain of the experimental data.

Note.

It will be necessary to make frequent reference to published and unpublished reports which are in the hands of the Committee. For convenience these will be now listed and given a reference letter.

A.- Report and Statement of Dr. Robert A. Kehoe to the Surgeon General's Conference in May 1925.

B.- A Study of the Hazards Associated with the Sale and Distribution of Ethyl Gasoline; by R. A. Kehoe and Graham Edgar, June 1925.

C.- A Study of Possible Health Hazards Arising from the Use of Tetraethyl Lead in the Automobile, by F. B. Flinn, Ph.D., May, 1925.

D.- The Excretion of Lead by Normal Individuals, by R. A. Kehoe, Graham Edgar, &c.
Journal American Medical Association, Vol 87, page 2081, 1926.

E.- Public Health Bulletin No. 163, published by the United States Public Health Service, and entitled "The Use of Tetraethyl Lead Gasoline in its Relation to Public Health," 1926.

F.- Report of the United States Bureau of Mines, entitled "Experimental Studies on the Effect of Ethyl Gasoline and its Combustion Products", 1927.

G.- A Study of the Health Hazards associated with the Distribution and use of Ethyl Gasoline, by R. A. Kehoe, M.D., &c 1927.

H.- Studies on the Absorption of Lead from Ethyl Gasoline by R. A. Kehoe, M.D., &c 1926.

I.- Addendum to "H" March, 1928.

J.- The Behaviour of Lead in the Animal Organism by R. A. Kehoe, and F. Thamann, 1928.

K.- The Problem of Automobile Exhaust Gas and Repair Shops of Large Cities, by J. J. Bloomfield and H. N. Isbell, U. S. Public Health Service, 1928.

L.- Lead Poisoning, by Aub, Fairhall, Minot, and Reznikoff, 1926.

M.- Lead Poisoning and Lead Absorption, by T. M. Legge and K. W. Goadby, 1912.

N.- Noxious Gases by Henderson and Hazard, 1927.

(2) History of Medical Investigations, U.S.A.

In October, 1923, an agreement was made between the U.S. Bureau of Mines and the General Motors Research Corporation that the former should carry out an extensive investigation on the toxicity of exhaust gases from motors using tetraethyl lead. This investigation was begun in 1923 and was continued through August 1925. The Bureau of Mines was later requested by the Ethyl Gasoline Corporation (formerly the General Motors Chemical Co.) to extend its investigations to a study of absorption by the skin and inhalation of vapour, and these investigations were begun in 1924 and completed in 1925. The entire data are published in Reference "F".

In June 1924, the General Motors Chemical Co. (later the Ethyl Gasoline Corporation) arranged with Dr. Robert A. Kehoe, Associate Professor of Physiology of the University of Cincinnati, to spend a part of his time carrying on, in co-operation with the Company, investigations on the whole subject of the Medical Aspects of Tetraethyl Lead. Investigations carried out by Dr. Kehoe and others are reported in reference "A", "B", "D", "G", "H", "I" and "J".

In the latter part of 1924 the Ethyl Gasoline Corporation invited Assistant Professor F. B. Flinn, of Columbia University, to carry out certain experiments on the effect of skin absorption and inhalation of petrol containing tetraethyl lead (Ref "C").

In October 1924, there occurred at a semi-works plant Bayway, N.J., engaged in the development of a new process for the manufacture of tetraethyl lead, a number of cases of poisoning and five fatalities. Because of the severe mental symptoms accompanying most cases of acute lead poisoning (from any compound of lead) a daily paper reporting the fatalities at Bayway coined the phrase "Looney Gas" in describing tetraethyl lead, and bearing in mind

that petrol in the U.S.A. is called "Gasoline" commonly abbreviated to "Gas", it was natural that the Press and the Public should associate the fatalities at Bayway with the use of Ethyl Gasoline (with which, of course they had nothing to do), and in fact this impression became widely prevalent. Confusion of Ethyl Gasoline with pure tetraethyl lead still persists in many quarters. Wide publicity followed the matter and several American cities took steps to prohibit the sale of Ethyl Gasoline. The matter was taken up by the United States Public Health Service, under Surgeon General Hugh S. Cumming, who called a conference for May 20th, 1925, to consider the entire subject. Although the results of the investigations carried out up to this time and those of the U.S. Bureau of Mines had indicated no hazard to the Public Health from the use of Ethyl Gasoline, the Ethyl Gasoline Corporation voluntarily suspended the sale of Ethyl Fluid to Oil Companies on May 5th, 1925, pending a decision on the matter by the Public Health Service (Ref. "E" P.V.). It was recommended at the Conference of the Surgeon General to investigate the entire subject and to report to a similar conference. Accordingly a Committee of seven scientists was appointed (Ref. E. P. VI) to carry out such an investigation. This Committee completed its investigations on January 17th 1926 and on January 19th 1926, a second conference was called at which there were present numerous representatives of industry, public health, science, engineering and medicine (Ref. "E", P. VII). The Committee reported (Ref. "E" P. 103) to the conference that in view of their investigations there were "at present no good ground for prohibiting the use of ethyl gasoline of the composition specified as a motor fuel, provided its distribution and use are controlled by proper regulations". The report was unanimously adopted by the conference. In accordance with these recommendations regulations were drawn

up by the U. S. Public Health Service in regard to the manufacture, distribution and use of tetraethyl lead and mixtures containing tetraethyl lead. These regulations were agreed to by the Ethyl Gasoline Corporation, the sole distributors of Ethyl Fluid, and a clause in its contract with its Licensees contains the phrases: "(b) Further, Licensee agrees to acquaint itself and comply with all rules and regulations issued from time to time by the office of the Surgeon General of the Public Health Service, the Department of Health of the State and/or Municipality wherein the business is carried on and any other Governmental agency having jurisdiction in the premises, relative to the handling and mixing of the antiknock compound and the distribution and sale of gasoline containing said antiknock compound." A similar clause covers the sale of Ethyl Petrol in England and the regulations of the U. S. Public Health Service are therefore observed.

The Regulations of the Surgeon General were presented on May 25th., 1926, for possible adoption and enforcement, to the Conference of State and Territorial Health Officers (Ref. "E" P. VII). It may be noted that so far as the writer is aware no legislation has been enacted looking to the enforcement of these regulations since the action of the Ethyl Gasoline Corporation, noted above, has given an effective means of their enforcement.

Following the Report of the Investigating Committee, The Ethyl Gasoline Corporation resumed business in May, 1926, and with one exception all prohibitory regulations concerning Ethyl Gasoline were withdrawn by such cities or states as had enacted

them.

Since the Investigation by the Committee appointed by the Surgeon General, the Ethyl Gasoline Corporation, with the co-operation of the University of Cincinnati, and always under the direct supervision of the Public Health Service, has undertaken to carry out each year, for an indefinite period, an investigation along the same lines as that carried out by the Surgeon General's Committee. The Results of this Investigation for 1926 are contained in Ref. "G". The results for the Investigation for 1927 have just been completed and will be presented to the Committee of Enquiry as soon as they can be obtained from America.

In addition to these investigations Dr. Kehoe and his associates have carried out and are continuing many experiments involving animals and these have yielded valuable information on many aspects of the problem. Such data are contained in Refs. "A", "H", and "I".

(3) Important Facts Developed by the Investigations.

It is obviously impossible to do more in a brief space than to touch upon the more important facts developed by the investigation, and even the particular points selected by the writer for consideration may not appeal to others as especially important. Nevertheless, certain facts are discussed briefly in the following paragraphs.

(a) Animal Experimentation.

Animal experimentation has been carried out with reference to possible dangers from exhaust gases; to the possibility of absorption of lead by skin contact and to the possibility of absorption of lead by inhalation of vapours. The experimental data involving concentrated tetraethyl lead or Ethyl Fluid will not be considered herein, as these do not concern the General Public, except to point out (Ref. "A" P. 2) that "comparison of the

that in general these are of the same order of magnitude. An exception of sufficient magnitude to be outside the limit of chance variation is seen, however, when one compares the poisonous character of lead salts taken by mouth with that of tetraethyl lead taken in the same way. In this case the salts of lead are seen to be about three times as toxic as tetraethyl lead. This is probably due to the greater ease of absorption of lead salts from the alimentary tract. On the other hand lead salts are not absorbed in lethal doses from skin, whereas death may readily be produced by the application of tetraethyl lead to the skin." In view of the tendency from some quarters to attribute to tetraethyl lead a unique toxicity, these facts are of importance.

In general most investigators seem to concur in the belief that it is extremely difficult to interpret the results of animal experimentation in connection with experiments involving tetraethyl lead diluted with petrol to one part in 1000-1500, partially because only very slight effects are to be looked for and partially because of the difficulty in designing an experiment which shall have a reasonable relation to the exposure to which a human being is apt to be subjected. The point is discusses in Refs. "a" P. 19a, "C" P. 13, "F" P. 143, "E" P. V, "H" P. 5.

As an illustration of this difficulty the problem involved in skin exposure may be cited. It appears a simple experiment to apply Ethyl Gasoline to the skin of an animal and determine in time whether repeated application results in storage of lead. Unless proper precautions are taken, however, the animal promptly licks the skin to which the gasoline was applied, and thus incurs an additional exposure to which a human subject would not be exposed. It is clearly necessary to have complete control of the conditions of such experiment, and also to maintain a group of similar animals treated with gasoline alone, for comparison with the test group. Little attention can be paid to uncontrolled experiments and it is not surprising that different experi-

mental work has not always been in agreement.

The main conclusions which have been reached are;

(1) (Ref. "F" P. 19) Some animals subjected to prolonged exposure to Ethyl Gasoline in a concentration of 0.1% in air showed storage of lead, though no characteristic symptoms of lead poisoning were noted (P. 21). The prevailing concentration of gasoline vapour around filling stations is only .01 - .03% and employees are seldom exposed to as much as 0.1% and then only momentarily.

(2) (Ref "H" P. 38) Under conditions which allow for spillage and evaporation of spilled gasoline leaving tetraethyl lead and dust of the decomposition products of tetraethyl lead, and which provide for regular skin contact and some ingestion of lead, such experimental animals as guinea pigs and rabbits do not give evidence of accumulation of lead in their bodies. Further, these animals, as well as monkeys, show no evidence whatever of injury to any of the functions normal to such animals, including reproductive functions, as a result of such treatment.

(3) In concentrations not exceeding one part of lead tetraethyl to 1000 parts of gasoline (the maximum concentration employed commercially is 1 - 1300), there is no evidence that rabbits absorb sufficient lead to cause accumulation of lead in their tissues. There is no selective absorption of lead under these conditions. (Ref. "H" P. 38).

(4) In connection with the exhaust gas problem it is possible to duplicate more exactly the maximum exposure to human individuals, since the experimental conditions are more similar. It is especially important to note the experiments of the United States Bureau of Mines in this question. Here animals were exposed from 3 - 6 hours per day to exhaust gases from an engine burning Ethyl Gasoline. The gases were diluted with air only to the point where the animals could exist without carbon monoxide poisoning. By using a very lean carburetter setting it

was possible to make this silution only 170 - 1; so that the experiment was much more severe than would have been the case had the normal carburetter setting been used, since in this case a dilution of about 400 - 1 would have been necessary. The results of these experiments showed that no storage of lead was found, nor any symptoms of lead poisoning after a period of nearly 8 months (Ref "F" P. 14-15). With the exception of symptoms of intercurrent disease (distributed impartially among controls and test animals), the animals at the conclusion of the test were healthy, lively, and had good appetites.

Altogether it may be said that the results obtained with animals may be taken as indicating that a health hazard from the use of Ethyl Gasoline is improbable, but this could not be taken as conclusive without considering the experience of human beings with the fuel.

(4) The Effects of the use of Ethyl Gasoline upon Human Beings.

All of the investigations on this subject have followed the same general line of attack, namely, to select different groups of men who have been exposed as severely as possible to the use of Ethyl Gasoline in one way or another. Similar groups of men who have not used Ethyl Gasoline in any way have been taken as controls. These two groups of men have then been subjected to the most rigid and searching medical examination (including the analysis of the excreta for traces of lead) with special emphasis on such signs and symptoms as may be taken to indicate storage of lead or incipient lead poisoning. The exact details of method in these investigations have varied somewhat but the plan has been essentially the same. In all of the investigations except the first there has also been included a third class representing men who are exposed to one of the many real industrial lead hazards. These men were selected as being almost certain to store some lead, yet not enough to give them the usual accepted signs of lead poisoning, and the object of including them was to make sure that

the medical examination was sufficiently rigid to be certain of detecting even incipient ill effects from lead.

The first investigation was carried out in the spring of 1925 by Dr. Kehoe and his associates (Ref. "B"): the second by the United States Public Health Service (Ref "E"): the third by Dr. Kehoe and his associates under the supervision of the United States Public Health, Service (Ref "G"): while the fourth, carried out similarly, has just been completed and will be available shortly. Several hundred men have been involved in each investigation.

Certain important facts have been established as a result of these three investigations. Among them are:

(a) A very large proportion of all normal individuals are exposed to lead in one way or another to such an extent that they are excreting small amounts of lead in the faeces or urine or both. (Ref. "B" P. 28, "D" p. 9, "E" P. 88, "G" P. 44).

(b) No individual person in any of the groups investigated gives evidence of lead poisoning or any other injury to health resulting in any way from Ethyl Gasoline.

(c) Workers in garages are commonly exposed to an appreciable extent to lead in one form or another, irrespective of their contact with automobiles using Ethyl Gasoline. Thus lead was found in the dust on work benches, floors, etc., in garages in which Ethyl Gasoline had never been employed (Ref. "E" P. 27-99). As an undoubted consequence, garage workers as a class show greater excretion of lead, on the average, than does the "Normal Individual" but not enough in any case investigated to indicate poisoning from lead.

(d) The men exposed to a definite lead hazard are differentiated sharply

group, showing that the medical examination employed was sufficient to show lead poisoning if it were occurring.

(5). Discussion of Experimental Findings.

In the foregoing pages the writer has confined himself to some of the more important experimental results of the various investigations. In the following paragraphs will be given a further discussion of some of the points in question, respecting the writer's own interpretation of the data. He has been closely associated with nearly all of the investigations cited, and therefore feels justified in presenting his own interpretations of them.

For such interpretations the original investigators cannot, of course, be held responsible.

(a) The exposure of normal individuals to lead.

Although the older literature on lead does not give much attention to the exposure to lead outside of certain recognized occupations, it must be realised after consideration that any member of a modern civilized community is of necessity exposed to lead from a number of sources, and apparently this has not affected the public health in any detectable way. Thus the dust from city streets has been shown invariably to contain lead; drinking water, because of the prevalence of a certain amount of lead piping, almost invariably contains lead (Ref. "E" p. 48); lead oxide is commonly employed in joining pipes; solder contains lead; lead paint is largely employed, and many other uses are common. It is thus reasonable to expect that the average individual excretes lead, and the presence of lead in the excreta cannot be taken in any way as indicating lead poisoning or danger of lead poisoning.

The human body is evidently able to handle without injury certain amounts of lead (Ref. "M") and the entire question in the use of Ethyl Gasoline is not whether there may be any exposure at all to lead, but whether such exposure is sufficient to bring the normal exposure up above the danger point. At present the answer would seem to be in the negative.

(b) Theoretical Hazards from the Use of Tetraethyl Lead.

From theoretical considerations many lurid pictures have been drawn by the imaginative as to the dangers which might result from the universal use of Ethyl Gasoline as a motor fuel. The most common of these involves the exhaust gases. These forecasts have been divided into several classes.

In the first class, lead dust is pictured as accumulating in the city streets to a point where eventually in years to come, there would be layers

of lead dust everywhere and lead poisoning would be general. Such a picture assumes apparently that dust is never removed by rainfall or street cleaning. Any rough estimate of the amount of dust and debris removed annually at present from the streets of a large city gives an enormous figure compared with the lead that it would contain if every motor car used Ethyl Gasoline.

A second picture is sometimes drawn of the driver of a motor car or the pedestrian on the road inhaling enough lead from exhaust gases to produce ill effects. Here again some quantitative figures are available. A rough idea of the dilution of automobile exhaust gases can be made by comparing the average and maximum concentrations of carbon monoxide which has been measured in the air in heavy traffic. The exhaust gas average of carbon monoxide is about 700 parts per 10,000; the average figure for heavy traffic is 0.78 parts per 10,000 and the maximum figure 1.66 per 10,000 (Ref. "K"). These represent dilutions of about one to 900 and one to 400 respectively of the exhaust gas with air. Experiments have shown that on the average, from an engine burning Ethyl Gasoline, about 25% of the lead may enter the exhaust gases in a form sufficiently finely divided to float for a time in the air. (Only a small fraction of the most finely divided dust is retained by human beings - Ref. "F" p.114). Taking the maximum figure for the tetraethyl lead used commercially, and assuming the average figures for the volume of exhaust gas from a gallon of gasoline (Ref. "F" p.47) we find that the concentration of lead in the air under the extreme conditions above cited, is roughtly 0.3 milligrams per 10 cubic metres of air, as an average, and 0.8 milligrams per 10 cubic metres for the maximum. Comparing these figures with the data of Legge and Goadby (Ref. "M"), who give 5.0 milligrams per 10 cubic metres as the minimum concentration apt to produce lead poisoning if breathed indefinitely every day, it is clear that we should not

expect, even under the worst possible conditions, with every automobile using Ethyl Gasoline, to obtain lead poisoning from exhaust gases, and this is in accordance with the results of the medical investigations.

Other pictures are sometimes drawn as to the dangers which might arise were Ethyl Gasoline allowed to evaporate on the skin, or spilled at a filling station. The relative rates of evaporation of gasoline and tetraethyl lead from Ethyl Gasoline follow well known physicochemical principles (Ref. "F" p.138 &c.). At first the more volatile part of the gasoline evaporates, containing no measurable amount of lead. (Thus during can and tank filling no hazard can arise, since a very small percent of the gasoline is evaporated under these conditions.) As the evaporation proceeds, the tetraethyl lead also begins to evaporate, and although the concentration of tetraethyl lead in the last remaining gasoline may be of a considerably higher concentration than the original concentration all of it must evaporate finally with the last traces of gasoline or at least it must remain in such small amount as to have a negligible physiological effect (Ref. "A" P.1).

(c) Regulations for Use of Ethyl Gasoline.

The Regulations proposed by the Surgeon General concerning the use of Ethyl Gasoline (Ref. "E" P.122) seem to the writer to embody sound common sense in every way. It must be realized that such warnings as "avoid spillage" &c. will undoubtedly be many times disregarded, and undoubtedly have been disregarded repeatedly, and the fact that no harm appears to have developed would indicate that such warning is not imperative; nevertheless, it is good sound advice as applied to Ethyl Gasoline or any other Gasoline. Spillage involves waste, fire hazard, and danger of ill effects to health from any gasoline (Ref. "H"; "F" p.21; "E" p.123) while such motor fuels as benzol and benzol blends are apt to be quite injurious to health

(Ref. "N" p.162; "F" p.27) through skin exposure or inhalation. Spillage of any motor fuel should be avoided.

With reference to Garages, &c., it has been shown (a) that dangerous concentrations of carbon monoxide frequently exist (Ref. "K" and that lead is commonly found in considerable amounts in the dust of all garages (Ref. "E" p.97 and 99). Such regulations concerning ventilation and cleanliness as those in Ref. "E" p.123 seem therefore desirable irrespective to the matter of Ethyl Gasoline.

(d) It may be of interest to point out that it has been the experience of the Ethyl Gasoline Corporation that when Ethyl Gasoline has been introduced into new territory numerous reports of alleged injuries from its use have arisen, while from territory in which its use has been extensive such reports are negligible. These reports have been thoroughly investigated whenever possible and in no case has there been any substantiation of the rumour that any injury could be traced to the use of Ethyl Gasoline. The Ethyl Gasoline Corporation's experience in this matter have been similar to that of the U. S. Public Health Service (Ref. "E" P. 39).

6. Unofficial Experiments in England.

There has been recently published and is still appearing in a daily paper the result of an investigation carried out in this country by Dr. Myer Coplans. This investigation will doubtless be given consideration by the Committee, and needs no particular discussion by the writer; nevertheless certain comment may not be inapropos. In this investigation two mechanics who had for a short while serviced cars using Ethyl Petrol were subjected to medical examination. One of them was found to be excreting a small amount of lead, and certain changes in the blood picture of both mechanics were reported. It is only necessary in discussing such data to

point out (a) that apparently neither man was examined before the test and their physical condition at that time is, therefore, unknown; (b) that small amounts of lead in the excreta is a quite normal occurrence and has no necessary connection with the test;(c) that changes in the blood picture of the order specified have no significance in themselves; and (d) that no control subjects were examined. It appears to be clear that no conclusions whatever can be reached from consideration of data so fragmentary. In addition it is shown that small amounts of lead were found on the overalls of the mechanics. In view of the prevalence of lead in all garages, as discussed above, there is again no necessary connection with the use of Ethyl Petrol and no particular significance in the findings.

These data, as few as they are, are the only ones having any particular importance; the remainder of the report in question is confided entirely to analytical data of doubtful significance, to discussion of industrial lead poisoning, and to speculations of the type outlined above concerning what might happen were the use of Ethyl Petrol universal. It would be easily possible to point outnumerous inaccuracies in the report, but considering the remote connection of the data in question with the subject of Ethyl Petrol this seems hardly worthwhile.

It is clearly that not by such methods as this that the possible health questions involved in the use of tetraethyl lead in motor fuel can be answered.

In conclusion the writer desires to express to the Committee of Enquiry his appreciation and that of the Ethyl Gasoline Corporation of the courtesy which the Committee has extended in permitting the presentation of this report, and to reiterate his desire to aid as far as may be in his power the establishment of the true facts concerning the matter under investigation.