

January 4, 1946

Mr. T. R. A. Bevan,
The Associated Ethyl Company Limited,
Artillery House, Artillery Row,
London, S. W. 1.

Dear Ray:

Quite some weeks ago in letters dated August 31 and September 21, I received from Fossett analytical data from Abadan as forwarded by Mr. Harrison. Fossett's original letter of August 31 was accompanied by a letter from Mr. Harrison dated July 26 in which there were a number of comments and questions, which I have attempted to deal with in a memorandum which you can deal with in accordance with your best judgment.

I regret that it has taken me so long to get around to this matter. However, there have been so many things to do that I have had to take them in accordance with their apparent urgency. I hope you will be able to convey this to Mr. Harrison in such a way as to indicate that I have not been unmindful either of their interests or of their very splendid cooperation. It is rather that I have not solved the problem of being in two places at once or of doing two things simultaneously. Perhaps the scope of the memorandum, attached herewith, will both explain my delay, and make amends for it.

With kindest personal regards,

Sincerely yours,

Robert A. Kehoe, M. D.

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MEMORANDUM ON REPORT AND QUERIES FROM ABADAN

Lead Exposure Associated with Various Occupations

The data obtained by the analysis of the urine of workmen have been examined, and various aspects of the problems involved, as raised in Mr. Harrison's letter to Mr. Fossett dated 26 July 1945, have been considered. The data are set up in tabular form herewith for illustration and comment, but the several occupational groups are referred to separately for greater clarity.

Distribution of Analytical Results Obtained Upon Samples of Urine of Various Groups of Workmen at Abadan in 1944 and 1945

<u>Urinary Lead Concentration</u> <u>Mg./L</u>	<u>Frequency of Occurrence of Analytical Results within Limits Indicated</u>						
	<u>1944</u>				<u>1945</u>		
	<u>Entire</u> <u>SEB</u>	<u>Nov. and Dec.</u>	<u>DF</u>	<u>TPA</u>	<u>SEB</u>	<u>DF</u>	<u>TPA</u>
0 - 0.019	1						
.02	11		9	2	1	1	1
.04	19	4	6	2	10	2	7
.06	23	1	6	8	6	4	6
.08	4	2	1	3	2	4	4
.10	13	5	6	5	12	8	3
.12	21	9	2	12	10	7	7
.14	7	2		4	2	2	3
.16	3			3			
.18	1	1		1			
.20	1			2	2		
.22				2			
.24	1						
Total	105	24	30	44	45	34	31
Mean	0.092	0.111	0.067	0.120	0.099	0.092	0.092
P.E.	±0.003	±0.005	±0.004	±0.005	±0.004	±0.004	±0.004
S.D.	±0.046	±0.035	±0.034	±0.049	±0.041	±0.036	±0.036
C.V. (%)	49.74	31.89	50.25	41.06	41.07	38.87	39.21

Mixing Plant Personnel

The group of men engaged in mixing Ethyl fluid with gasoline deserve special attention in view of the data and the question raised as to the accepted limit of safety:

1. The data on these men (Class S.E.B.) demonstrate clearly that some degree of occupational lead absorption is occurring among them. The comparison of the available data for 1944 with those for 1945 shows that no significant reduction in the lead exposure has occurred during 1945, even when one employs the results obtained only for the months of November and December of 1944 (by which time most of the low results due to the introduction of new men with no prior occupational lead exposure during earlier months of the year, were eliminated).

2. Examination of the results on individual men for the year 1945, show that eight members of the group have provided more than one sample with a lead concentration in excess of 0.10 mg. per liter (Case 93, 129, 130, 141, 142, 143, 152 and 166), and that these men appear to be more or less consistently high in their rate of lead excretion. One (#166) had two dangerously high results, while another (#152) had the highest of all (0.32 mg. per liter), followed subsequently by a lower but significant result (0.13 mg. per liter). There may have been some factor of contamination to raise the general level of these results, but one may not safely assume that this was the case.

3. The question of the tolerable or safe limit of lead exposure, as expressed in terms of urinary lead excretion, appears not to have been fully understood, and in a subsequent part of this memorandum I shall attempt to clarify this matter and to give advice on the application of suitable criteria for the disposition of individual cases. However, this is not the point involved in the operation of plants in which Ethyl fluid is mixed with gasoline.

Persons who work with Ethyl fluid in its concentrated form

must be protected against lead exposure. Unless they are protected completely, it is not possible to be sure that they are protected at all, for the rate of lead absorption as the result of contact of the skin with Ethyl fluid or because of inhalation of vapor given off from the concentrated fluid, is so rapid as to be excessively dangerous. Errors of technique or judgment, therefore, may have prompt and serious results. Accordingly, a regimen of precautions, in the form of suitable equipment and detailed instructions, has been provided, which has as its purpose the avoidance of all exposure and all absorption of lead. Moreover, evidence of lead exposure and absorption on the part of the workmen, is regarded as evidence that the mixing equipment is inadequate, or that the instructions are not followed properly, or that both of these factors are involved. When such evidence is available every effort must be made to find the faults in performance and correct them. It is not a question, therefore, of how long a man can work in this occupation, or when he has been exposed for a period sufficiently prolonged to be dangerous. It is rather a question of whether he has been trained sufficiently (or well enough supervised) in the performance of his duties so as to avoid lead exposure.

Recognizing the fallibility of man, some provision has been made for offsetting the effects of some slight defects in the precautions. Therefore, the periodicity of mixing operations has been regulated. This regulation has certain other purposes, however, which are more important than the spacing of exposure. It also has a tendency to determine the character of the mixing equipment. Our reasoning in this regard takes the following line; - if it is necessary to mix more frequently than six times per month, then the mixing equipment is not of the type best adapted to the purpose. In general

our experience fully justifies this conclusion. Therefore, (to answer another question in Mr. Harrison's letter), the duration of an individual mixing operation is not a primary consideration, and we are not in position to take it into account. We must insist upon the importance of the avoidance of lead exposure. If that is done the length of this time is unimportant. Moreover, it is not our general practice to make use of multiple groups of men, so as to limit individual exposure. Instead we insist upon changing to a type of equipment that requires no limitation of the frequency of mixing.

It is recognized that these principles are not now applicable in every respect at Abadan. A large volume of fluid in drums must be handled, and the long time and the frequent repetition of this work introduce some degree of hardship and discomfort into the work of the men, as well as some tendency for relaxation of precautions. This elsewhere, at least in the U.S.A., would be counteracted by the adoption of a new type of mixing equipment which would enable the Ethyl fluid to be handled in bulk under conditions which, during mixing, would entail no opportunity for lead exposure. The one most important principle, however, does apply at Abadan, and indeed, is all the more imperative, - namely the principle of complete avoidance of lead absorption. So long as we cannot apply the orthodox solution of this problem, in the form of new equipment, it is necessary that every other means for the avoidance of exposure be emphasized. For this reason, the use of multiple crews of mixing personnel was approved.

For the above reasons, the relaxation of the standard of safety as expressed in urinary lead concentration, in this occupation,

is not good policy or practice. What I said of this originally in Abadan in relation to mixing, was that lead concentrations in excess of 0.10 mg. per liter of urine were almost certainly indicative of occupational lead absorption even though there were only a few results to go on, and as such were to be regarded as dangerous, not in themselves, but rather because they demonstrated failure of the precautionary regimen. This is true now, as it was then. The criterion of "safe" versus hazardous lead absorption (to be discussed later), is applicable in industries in which there is a slight or moderate, conventionally controlled hazard. It is not applicable to this occupation, in my opinion. Rather, the evidence of lead absorption on the part of these workmen, is proof that the entire operation needs better and closer supervision or better equipment and operating methods. It is a sign of need for improving the performance, not for changing the program of medical handling of the men.

Drum and Can Filling Personnel

It is obvious that work done by these men involves some degree of almost unavoidable lead exposure, which, however, can be accepted with a degree of equanimity because of certain factors which operate without fail to dilute the exposure and to make it less than immediately hazardous. (1) The dilution of the lead compound with gasoline reduces the danger of fatal skin absorption of T.E.L. to the vanishing point, and decreases the volatilization of T.E.L. in an indirect manner. (2) The presence of gasoline liquid and vapor, introduces other obvious risks (fire and explosion) the control of which tends to reduce greatly the lead exposure.) One is not likely to be poisoned by T.E.L., therefore, in these occupations, as the result of an accident or a technical error that gives rise to a

brief exposure. Poisoning, if it can occur under existing conditions, results from relatively prolonged exposure, which therefore provides time in which to appraise the situation and to take appropriate action. It is in such a situation that the level of the lead excretion of groups or individuals demonstrates that the sources of lead exposure require better control if conditions are to be safe for indefinite periods of employment, or alternately, that an individual needs to be removed from exposure for his own safety.

In dealing with problems of this type we have found by experience that if the stable mean concentration of lead in the urine of exposed workmen does not exceed 0.10 mg. per liter, cases of lead poisoning will not occur. This same fact applies to the individual if there are a sufficient number of analytical results to provide a stable mean value for the expression of his actual physiological status with respect to lead absorption. (This implies, of course, that the lead exposure is fairly well controlled and not subject to wide variations from time to time. Otherwise stable mean values could not be obtained.) This standard allows for certain variations above and below the mean, and does not require that a man whose urinary lead concentration in a given instance, is above the mean value, is to be removed from his employment. On the other hand, the standard itself is factual, and as such is not subject to modification to meet a given set of practical conditions.

Looking at the tabulated data from this viewpoint, and assuming that there is no factor of contamination to elevate the individual results and thereby the mean values, the following conclusions are justified;

1. The lead exposure associated with drum and can filling was kept within safe limits during 1945, but was just at the threshold of danger, i.e. there is no large factor of safety.

2. If, however, conditions remain as they are, it is possible that the factor of time and lead accumulation in the tissues of persons who remain in their respective occupations, will cause the mean values to increase to levels that will then be unsafe.

(We have previously discussed the special factors in connection with the mixing of Ethyl Fluid with gasoline, which negate the conclusion that this occupation is safe, or, at least, that it would be so considered under the usual conditions of unsupervised work, that normally characterize this work in various parts of the world. However, it can now be said that if the supervision of this work is or should be sufficiently precise and continuous so as to prevent all highly dangerous exposure to T.E.L., this same conclusion is applicable here, as it is in T.E.L. manufacturing plants, where supervision is continuous, and where the training and discipline of operating personnel is kept at a high level of quality.)

Criteria for the Medical Handling of Exposed Personnel

Over the years of observation and study of conditions and personnel in manufacturing operations, criteria have developed which enable the physician to determine how to deal with the several situations which arise in connection with the safety of individuals. The special conditions of the war-time manufacture of tetraethyl lead have given to these criteria a precision that was formerly lacking. It is to be remarked that there is no large factor of safety in their application, in view of the fact that shortage of men in the manufacturing plants was responsible for the exercise of the most conser-

vative judgment in the removal of men from their employment. At the same time, it may be said that not even the necessities of war were believed to justify the acceptance of undue risk on the part of individual workmen. Therefore, these criteria are advanced with some confidence in their validity.

1. When analytical data are available in the presence of symptomatology of any type,
 - a. the symptomatology should be interpreted without reference to analytical data and a conclusion arrived at as to its significance, taking into account the hematological and other laboratory findings;
 - b. a cause and effect relationship between lead absorption and non-specific symptomatology, on the part of men who have been working up to the time of sampling, may be excluded, when
 - (1) the results on a sample of blood and a spot sample of urine are well within safe limits, i.e. - less than 0.06 mg. per 100 grams of whole blood less than 0.12 mg. per liter of urine; or when
 - (2) repeated results on spot samples of urine are within safe limits as defined above, or when
 - (3) the result on a large sample of urine is within safe limits as defined above.
 - c. a cause and effect relationship between lead absorption and non-specific symptomatology may be assumed to exist, when
 - (1) other causes of symptomatology have been excluded beyond reasonable doubt and the analytical results are above safe limits; or when
 - (2) the background of the symptomatology is quite uncertain, and the analytical results are within the dangerous range, i.e. -
0.08 to 0.15 mg. per 100 grams of whole blood
0.18 to 0.40 mg. per liter of urine.
 - d. a cause and effect relationship between lead absorption and strongly suggestive or specific symptomatology may be assumed to exist, when
 - (1) the analytical results are within the dangerous range; or when
 - (2) it is known that the analytical results were well above safe levels during a period of lead exposure that has now been discontinued for some weeks.

2. When no symptoms of any kind exist, persons should be removed from lead exposure or transferred to work involving greatly reduced exposure, when

a. the analytical results are consistently within dangerous limits, i.e. -

- (1) results on a blood sample and a spot urine sample are in agreement at high levels of more than 0.08 mg. per 100 grams of whole blood and more than 0.18 mg. per liter of urine; or
- (2) repeated results on spot urine samples are consistently within the high range indicated above; or
- (3) the result on a large sample of urine is within the range given above (0.18 mg. per liter or more). (An exception may be made in this rule when it can be established that a high result is of short duration and is followed by a rapid drop in the results, as in the case of brief severe exposure.)

3. Men with no symptomatology may be returned to the work from which they were transferred or removed because of excessive lead absorption, when

a. the analytical results have fallen to levels that are consistently safe, i.e. -

- (1) the blood results are down to 0.05 mg. per 100 grams or lower, and the urinary results are not higher than 0.10 mg. per liter; or
- (2) the results on urine samples of large volume (one liter or more) are not in excess of 0.10 mg. per liter, and a representative sample of feces for a twenty-four hour period contains under 0.40 mg. of lead. (In general, the length of the period of reduced or discontinued lead exposure should be more extended in the case of persons whose employment under conditions of potentially hazardous exposure has been prolonged, i.e. the longer the period of exposure, the longer shall be the period of freedom from exposure.)

Masks for the Protection of Mixing Plant Personnel against T.E.L. Vapor

Previous discussion of the hazards of mixing have dealt with the need for additional precautions. With respect to canister masks, additional comments are justified.

The standard prescribed in the instructions with reference to the length of use of canisters (100 hours) has been set up in relation to the somewhat diluted vapor of tetraethyl lead only. It

has no application to gasoline vapor, on which we have no valid data. In mixing operations, as we are generally familiar with them, the problem of concentrated gasoline vapor is not encountered to an important degree, and therefore we have not attempted to deal with it, in the belief that technical and medical personnel in the petroleum industry have had more experience with it than have ourselves. It is known, however, that moderately concentrated gasoline vapor will flood a canister mask and render it ineffectual after relatively brief periods of use. There is no means of dealing with this problem except experimentally. If and when exposure to gasoline vapors occurs to a significant extent in association with mixing operations, standards will need to be established and put into effect to meet the actual conditions. If possible, it is well to deal with the gasoline hazard as an entirely separate problem, and to limit exposure to gasoline in mixing operations to such an extent that the masks used against tetraethyl lead vapor will be directed solely against that hazard. If this cannot be done, a period of use of the canister will have to be set to meet the requirements of the most concentrated vapor, that of gasoline, in the mixture of vapors to which men are exposed.

Cumene

The toxic effects of exposure to cumene have not been fully investigated, so that it is not possible to set up a standard of safety for prolonged regular exposure. Work is under way at the National Institute of Health in Bethesda, Maryland, U.S.A., but has not been completed. Information on acute effects is available and a copy of a reprinted publication is enclosed herewith. It seems probable that the concentration of 50 p.p.m. is reasonably safe and it is not surprising that exposure to concentrations of several hundred

parts per million caused difficulty. The observations made at Abadan are of great interest, and the handling of the problem as indicated is cause for congratulation.

Signed: *Robert A. Kehoe*

Robert A. Kehoe, M.D.
Chief Medical Consul
Associated Ethyl Company, Inc.

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