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Mr. C.F. Reinhardt,
Haskell Laboratory,
E.I. Du Pont de Nemours & Company,
Wilmington,
Delaware 19898,
U.S.A.

Your ref.

Our ref.

12th March 1973

Dear Mr. Reinhardt,

Following an invitation from Dr. K. Bridbord to comment on the latest (November 29th, 1972) E.P.A. report on the Health Effects of Airborne Lead, I have forwarded to him a copy of the enclosed which I send to you for information.

As you will note from my remarks, I do not subscribe to many of the arguments, or to the conclusions that are reached in the E.P.A. document.

Yours sincerely,

(P.S.I. Barry)
Chief Medical Officer

PSIB/dl.

the contribution from lead in the air had been of material significance, in comparison with other possible sources, to the body burden of lead as represented by blood lead, then the New York group should have shown the higher values. The fact that they did not would seem a pertinent argument for supposing that an average city lead in air exposure of 2 $\mu g/m^3$ is of insignificant proportions compared to other avenues of exposure and absorption, such as from food and drink.

In Section II of the health report "Clinical manifestations of lead poisoning" it is inferred that children with blood lead levels below 40 µg/100 gm may be suffering from subtle, undiagnosed effects of lead poisoning, such as mental retardation and hyperactivity. The report does say that these effects "may have been present before lead poisoning occurred", but in so saying implies that lead poisoning was a feature, irrespective of the cerebral changes, although no other manifestations of lead poisoning in the children investigated were recorded. This seems to be begging the question and such a statement pre-empts a non-existent situation. The studies by David[2] and Moncrief[3], to which the health document refers, do not confirm that excessive lead exposure was a cause of the mental changes noted in the series of children investigated by them. The E.P.A. health report does draw attention to this point, but unemphatically, and one is left with the impression that, despite the doubtful evidence, the mental changes, in the view of the E.P.A., were caused by lead exposure.

There is no question that young children have been, and still are, at risk from the ingestion of lead-based paint flecks from the surfaces of old dilapidated buildings and from lead-based painted cots. These sources of exposure and intake have been well documented[4-7] and have caused frank clinical lead poisoning. They cannot however be associated with the general environmental air situation, which has not been shown to contribute, at a clinical level, to ill-health among any section of the population.

It seems unfortunate that confusion has been allowed to develop which might result in an indictment of a harmless general atmospheric lead level at the expense of allowing a number of serious specific sources of exposure to continue to exist.

Comments on the E.P.A's Position on the Health Effects of Airborne Lead (November 29th, 1972)

The intention of the E.P.A. in recommending a reduction of lead in gasoline appears to be with a view to the reduction of lead in atmosphere, and so to intake by the general population, in the anticipation that lower blood lead levels will result.

Whether in fact such an outcome would materialise from enforcement of the E.P.A. recommendations is a matter for present conjecture and future observation. In my view it is unlikely that a significantly measurable change in blood lead levels would follow.

It is indicated in the E.P.A. health document that ambient air lead concentrations of the order of 2 $\mu g/m^3$ contribute significantly to blood lead levels, to a point where a hazard to health may result.

This figure was calculated from a theoretical extrapolation of the Goldsmith - Hexter curve[1] and is not based upon controlled experimental findings. The officers of the E.P.A. will be well aware of the informed criticism that has been presented to them on this point.

To suggest that a hazard to health may arise, as opposed to a blood lead equilibrium of harmless proportions, from a continuous exposure to respirable lead in air of the order of concentration of 2 $\mu g/m^3$, belies an understanding or appreciation of the body's physiological response to lead absorption, hardly credible of the E.P.A. health authorities.

The contribution of lead in air, at concentrations commonly found in cities, to bodily absorption as represented by lead in blood, would appear, from the tabulated data in the E.P.A. health report, to be of minimal significance. From the Seven City study, reported in Table V-1, Section V, p.5 of the report, the data for the Philadelphia population, both urban and suburban, show a higher blood lead level than do the equivalent data for the New York population, although the air lead levels are marginally lower in the Philadelphia urban area. The Philadelphia urban and suburban populations show respective average blood lead levels of 20.5 and 18 $\mu g/100$ gm blood at air exposures of 1.67 and 1.15 $\mu g.Pb/m^3$, compered to the New York urban and suburban populations of 16.6 and 15.3 $\mu g/100$ gm blood respectively at air exposures of 2.08 and 1.13 $\mu g/m^3$. It would seem reasonable to expect that if

With respect to Section III of the E.P.A. health report, "Low level metabolic effects of lead", it seems to be accepted by the E.P.A. that ALA dehydratase activity and chromosomal changes may only be of significance in relation to health at very much higher levels of lead exposure than is currently experienced by the general population.

The physiological significance of reduced ALA-d activity at blood lead levels of 40 µg/100 gm and above has not been defined and workers such as Nikkanen and Hernberg[8] do not impute a health effect to their scientific observations. Furthermore it is known that other heavy metals such as zinc and copper[9] and also alcohol[10] exert an effect upon ALA-d activity so that this cannot be considered an effect specific to lead, a point which is not mentioned in the E.P.A. health document. ALA-d does not play any part in the physiological activity of whole blood. No in vivo work has been done and in the in vitro studies of blood samples at lead levels of the order of 40 µg/100 gm no abnormalitty in haemoglobin has been found. In view of the function of ALA-d in the haem synthetic chain one might have expected to have seen a change in haemoglobin if a reduced activity of ALA-d in blood in vitro was of important physiological consequence. Lead induced inhibition of ALA-d required for cytochrome synthesis in other tissues may reflect significant impairment, as indicated in the E.P.A. health document, but it would be reasonable to suppose that this could only occur at much higher, toxic proportions, of blood lead levels than is inferred by the E.P.A. At present any such outcome is purely speculative and has no support from in vivo experimental work which has yet to be undertaken.

The same could be said about any genetic implication of lead, particularly in respect to the low level exposure of the general population, where there is no evidence which might suggest that any such effect occurs.

With regard to Section IV of the health report "What is a safe blood lead level?", whereas it is reasonable to take a figure of 40 µg.Pb/100 gm blood as representing a level of lead intake below which no possible health effect could occur, the obverse, that any level above this figure is indicative of a significant exposure leading to lead poisoning, does not follow. Many adults

can tolerate blood lead levels in excess of 80 µg/100 gm without demonstrating toxic effects, as has been noted primarily among industrially exposed workers. A figure of 40 µg.Pb/100 gm blood is an essentially safe level and should not be regarded as a level bordering on intoxication. With respect to children a blood lead level of 40 - 50 µg/100 gm should be regarded as an indication of unusual exposure, but the evidence does not confirm that at these levels children are suffering from lead poisoning.

That children are more liable to ingest large quantities of lead, particularly in the one to three year age group, is not in dispute, for reasons that have been well documented[4-7,11]. The evidence does not suggest that, for a given dose on a weight for weight ratio, children are more sensitive in their response to lead than are adults. Because, however, of their greater potential for exposure and subsequent intake, resulting from an exploratory appetite, they are more likely to absorb large doses in a short space of time which can lead to toxic blood lead levels well in excess of 70 µg/100 gm, ending in a serious clinical condition of cerebral encephalopathy. For these reasons one might argue that children are more "susceptible" to dangerous levels of lead intake than are adults, but one should be careful not to interpret this as a physiological susceptibility or sensitivity to lead, peculiar to children, on a dose related basis. The impression given by the E.P.A. health report is that children are more physiologically susceptible to the effects of lead, but this is not confirmed by the documented child studies that have been undertaken.

The guidelines proposed in the health document of 40 µg.Pb/100 gm of blood for adults and children and 30 µg/100 gm for the foetus and new born children are reasonable as indications of levels at or below which no possible harm could occur. However, since these levels must have an essential built-in safety margin to be of any value as guidelines for the population as a whole, it is not reasonable to assume, as apparently the E.P.A. does, that at or above these figures a situation hazardous to health exists.

With respect to Section V of the health report "Sources of lead exposure among the general population", that automobiles emit particulate lead at the roadside is not in dispute. A higher

air lead exposure is to be expected immediately adjacent to a heavily trafficed roadway than at more distant points. The interesting finding, however, is the rapidity with which the air lead level reduces at short distances away from the roadway (Table V-1). As outlined in Table V-1, at air lead levels in excess of 2 $\mu g/m^3$ the blood lead levels of the populations studied were of the order of 17 µg/100 gm, a level well within safety margins with respect to excessive lead exposure. Even among people living within 12 feet of the roadway, at air lead concentrations in excess of 4 $\mu g/m^3$, blood lead levels still only measured 23 µg/100 gm, a figure that would not cause any concern in relation to health. It is respectfully suggested that people living as close as 12 feet from a busy highway would have justifiable cause for complaint, irrespective of what their blood lead levels might be!

As suggested earlier, the contribution of ambient air lead to blood lead, from the evidence outlined in the E.P.A. health document, appears to be of a very low order, and not comparable to other avenues of absorption from other sources.

With respect to the work by Dr. Coulston and his colleagues at Albany[12], referred to in the E.P.A. document, the blood lead levels of six prison volunteers did show an increase from 18 to 24 µg/100 gm throughout a period of 12 weeks exposure to a concentration of lead in air of 3.2 $\mu g/m^3$, for periods of 23 hours in every 24 hours. The E.P.A. health document report, however, fails to point out that the blood lead level of 24 µg/100 gm was reached after four weeks of exposure and thereafter did not increase, indicating that equilibrium was reached at a harmless level of lead in blood, despite a continuing constant air lead exposure of 3.2 $\mu g/m^3$.

There appears to be a correlation between the blood lead levels of people living 12 feet from a busy highway (Table V-1) and the prisoners in the Albany investigation. The blood lead levels achieved in these circumstances, however, cannot in any way be regarded as hazardous to health, a point that is not made clear in the E.P.A. health document.

With respect to the role that ambient air lead concentrations may play in the contamination of dirt and dust which might be

ingested by children in the "susceptible" one to three year age group, no evidence is forthcoming that this constitutes a serious source of intake in relation to excessive absorption, which might result in dangerous consequences to child health.

The causes of excessive and dangerous lead intake by children have been well defined[4-7,11,13], and are principally related to the presence of lead in paint. The contribution of lead in dust and dirt has not been adequately assessed and the National Academy of Sciences report of 1971[14] makes this clear while at the same time pointing out the known serious consequences afforded by the ingestion of lead-based paints among children living in low level socio-economic circumstances. The absorptive quality of lead in dust and dirt, as measured by degree of solubility, is probably of a much lower order than lead in paint, and thus of material clinical significance. It should be taken into account by the E.P.A. in any assessment of the relative importance of the contributions of lead exposure, from a variety of sources, in relation to a possible health effect. It does not appear from the health document that the E.P.A. has in fact reviewed all the available data adequately.

It is stated in the E.P.A. health document that 90% of the lead in the ambient atmosphere is derived from lead in gasoline. That lead in gasoline contributes to total atmospheric lead is not in question, but the level and health significance of the contribution most certainly is. In the first place a 90% contribution figure seems exaggerated and one might reasonably expect a considerably lower figure than this to be the true level of contribution. Also it has yet to be determined that lead from gasoline, in the form emitted at automobile exhaust tail pipes, is readily assimilated. The work of Lawther et al[15] provides evidence that lead from automobile tail pipes is of low absorptive quality. No other similar work has yet been undertaken, with particular application to auto exhaust, which might deny the findings of these researchers.

It appears to be inferred in Section V, p.11 of the health report, in quoting the work of Stara et al[16], that large numbers of urban children are ingesting 5 mg.Pb.per day in their diet, equivalent to 17 times the established average figure of 300 µg.Pb/ day ingested by adults. This would be a high level of lead intake

giving rise to a real risk of clinical intoxication. However, the evidence does not suggest that such a level of intake is a usual occurrence and the E.P.A, have no grounds for making implications to the contrary.

The same criticism might be levelled in respect of calcium deficient diets leading to increased lead uptake, at lead concentrations in the drinking water of 200 ppm[17] (E.P.A. health report, V, p.12). This concentration of lead in drinking water is some 2,000 times the W.H.O. recommended figure of 0.1 ppm and within a toxic range, irrespective of whether the diet is low or normal in calcium content. It is not reasonable to assume from this evidence, as the E.P.A. health document infers, that the movement of lead from bone either occurs or is a cause for concern in conditions such as pregnancy, where a higher than normal calcium requirement may be necessary.

With respect to the children under investigation in El Paso (Section V, p.13-14 of the E.P.A. health report), living in the immediate vicinity of a lead smelter, a number of factors need to be stressed which are omitted in the E.P.A. health document. First, none of the children demonstrated evidence of clinical lead poisoning. Secondly, a surprisingly large number in the age range 6 - 17 years demonstrated elevated blood lead levels, a finding not previously observed in other studies. Thirdly, the respirable airborne lead level to which this population was exposed (100 - 300 $\mu g/m^3$), even if 75% was judged to be in the non-respirable range, still exceeds ambient air lead levels in cities by 10 to 30 times. It would seem that air lead may have been a major contributor to the elevated blood leads seen in the El Paso group of children, with some confirmation provided by the high percentage (64.7%) of children between the age range of 6 - 17 years who demonstrated blood lead levels in excess of 40 µg/100 gm. However, this can only be a speculative surmise at the present time.

Nearly 90% of the one to five year old children demonstrated blood lead levels over 40 µg/100 gm, and yet the dust and dirt lead concentrations in the El Paso district in which the children lived were only 0.4% to 0.5% lead, comparable to the findings from many cities. Nowhere near 90% of children of this age group living in cities show blood lead levels in excess of 40 µg/100 gm.

The El Paso situation is a particular problem associated with proximity to a lead smelter and is not analogous to the contribution of lead from auto exhausts to the environment. As an in-depth study of the El Paso children is currently underway no conclusions should be drawn, or pre-emptive assessments made of the significance of the lead intake by this group, until such time as the study has been completed.

Section VI of the E.P.A. health report "Extent of abnormal lead exposure among the general population" draws attention to the data outlined in Table VI-1. It is stated that "within each city in Table VI-1 the percentages of individuals with abnormally elevated blood leads are generally consistent with the expected gradients according to exposure category". This statement does not match up with the data given in Table VI-1, unless one is to assume either that the comparable Cincinnati groups were more heavily exposed to air lead than their counterparts in Los Angeles and Philadelphia (no air lead figures are quoted) or, if the air leads in the three cities were comparable, then the Cincinnati groups were more heavily exposed from other sources, such as from food and drink.

Another possible explanation may be in the differences in analytical results obtained between laboratories on blood samples containing the same quantities of lead[18], a problem of real material significance which is not sufficiently appreciated or adequately explored.

In the outline in Table VI-3 of the percentages of children with blood lead levels in excess of 40 µg/100 gm, little evidence for the source of the children's lead intake is provided by the data. For the New York children, however, the data is rather intriguing. Between 1969 and 1971 the percentage of children with blood leads in excess of 40 µg/100 gm more than halved (from 45.5% in 1969 to 20.2% in 1971). The same could not be said for traffic density which, if anything, probably increased during the period, so that the contribution of lead to air from auto exhausts cannot have decreased. Obviously there must be some other explanation for the reduction of blood lead levels observed in the New York children. Perhaps improved living conditions may have played a part, but it does not seem from this evidence that lead from auto exhausts is a serious cause for concern in relation to uptake of

lead by children.

The interpretation of the data on umbilical cord blood in the E.P.A. health document (Section VI, p.4 and 5) appears to be misleading in that the E.P.A. argue from the data that significant percentages of babies born in urban environments are probably exposed to excessive amounts of lead, as represented by blood lead values in excess of 30 µg/100 gm, even before birth. This is not the conclusion reached by the investigators in the three studies quoted by the E.P.A.[19-21].

The Boston study by Scanlon[19] comprised samples of umbilical cord blood from 13 infants born of urban mothers and 15 infants of suburban mothers (28 in total). Three of the urban infants showed umbilical cord blood sample values in excess of 30 µg/100 gm, but the author of this study did not find any statistically significant relationship for umbilical cord blood lead levels and residency during gestation in either city or suburbs. The mean umbilical cord blood lead values were 22.1 µg/100 gm for the urban group and 18.3 µg/100 gm for the suburban group. To quote from the Scanlon paper "The atmospheric lead concentration for urban Boston has a mean value of 2 µg/cu.m. of air, while the concentration in surrounding suburban areas averages at less then 1 µg/cu.m. These data suggest that the urban mother may have twice the atmospheric exposure to lead as the suburban mother. There is no indication from our results that Boston urban infants carry a significantly higher lead concentration than their suburban peers at birth, at least as measured by their umbilical cord blood levels." The E.P.A. appears to lean heavily, for the support of their arguments, on the finding that three samples of umbilical cord blood from urban infants in this study exceeded 30 µg.Pb/100 gm, although the author himself does not seem to consider this to be of important significance.

In view of the apparent dependence of the E.P.A. upon the Scanlon data, it seems strange that they should discount the study by Harris[20], who found no umbilical cord blood values in excess of 20 µg/100 gm in either urban or suburban groups, on the grounds that the total of babies sampled, numbering 24, was too small for valid statistical evaluation. The total of babies in the Scanlon study was 28. Do the E.P.A. suggest that the difference of four babies between the two studies provides a viable quantum for

statistical purposes, or could it be that the Harris study was not convenient to the E.P.A. argument?

The third study on umbilical cord blood by Rajagowda et al[21] to which the E.P.A. health document refers does not report, as is implied by the E.P.A., that any of the 100 samples obtained exceeded 30 µg/100 gm blood. The distribution of cord blood lead levels ranged between 0.01 mg to 0.03 mg/100 ml. Six of the samples showed values of 0.03 mg/100 ml blood, equivalent to 28 µg/100 gm blood. The E.P.A. document implies that the six babies born with umbilical cord blood of the order of 30 µg/100 ml all exceeded this level, which does not seem to be the interpretation given by the authors of this study. It would appear from the Rajegowda study that probably none of the samples exceeded 30 µg.Pb/100 gm blood, but that a small number may have reached this level, rather a different conclusion from that of the E.P.A. It might perhaps be cogent to the argument to quote as follows from the Rajegowda report "There is no evidence at this time that lead present in the atmosphere is harmful to the foetus".

Thus the conclusion of the E.P.A., as stated in the health document, that "considered as a group, these studies indicate the probable existence of abnormally elevated umbilical cord blood lead levels among babies born in urban environments" is not tenable, on more detailed study of the data than apparently was afforded by the E.P.A.

With respect to appendix A attached to the health document concerning E.P.A's conclusions from responses received to questions which appeared in the federal register of June 14th 1972, in my opinion insufficient attention was given by the E.P.A., in arriving at their conclusions, to the letter dated 26th July 1972 by Dr. Julian Chisolm addressed to Dr. Vaun Newill. In particular, Dr. Chisolm's remarks relative to Questions 2, 4 and 5 are of cogent application to the matter under review, but it does not appear from the E.P.A. health document of Nov. 29th, 1972 that his views, derived from a knowledgeable depth of practical experience, have been adequately considered and reported. A greater attention on the part of E.P.A. to Dr. Chisolm's views is to be commended.

To summarise, whereas one appreciates the difficulties and intricacies involved in the preparation of a report on the health effects of airborne lead, the report of Nov. 29th 1972 prepared by

the E.P.A. fails, in my view, to provide a true picture of the situation as it exists at the present time. The conclusions reached in the report are for the most part not tenable on the basis of the evidence available and appear to be derived largely from unsubstantiated theoretical considerations, based upon assumptive arguments.

I believe a greater emphasis needs to be placed upon the proper utilisation of the wealth of practical information that is already available, if meaningful conclusions are to be reached in respect to the health effects of lead upon the population, as a whole and in relation to particular segments. Only thus can responsible action be formulated and unnecessarily wasteful measures be avoided.

(P.S.I. Barry)

8th March 1973.

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