

September 20, 1971

Mr. David J. Miller
Suite 401
1010 Vermont Avenue, N.W.
Washington, D.C. 20005

Dear Mr. Miller:

First, let me express my thanks to you, again, for your courtesy (and the loan of funds) in the matter of the tickets for the opera on the evening of the 14th. It was a remarkable experience and, quite realistically, "out of this world."

The interview in your office was, I hope, helpful to you and, in some measure, a repayment. I say, "I hope," in terms of your task, which I know is a difficult one. Let me speak, once more, as to the basis of our experimental effort. In attempting to advise the group of persons and companies concerned with this type of hair dye, I first wished to know whether or not there is a real hazard to their customers in the use of these dyes. As a physician, with some knowledge and experience in the uses of lead in the modern community, I felt it incumbent upon me to know the facts and to give advice on that basis. I recognize, of course, the official responsibilities of the Food and Drugs Administration, and I should be pleased to have them confirm my view of the matter derived from which I consider to be a crucial experiment, but I conceive of my own responsibility as being quite as serious as theirs, in terms of the basis of my opinion. My colleagues and I, in the Netter Laboratory, over a period of years, have stood between segments of the American public and danger in a number of situations. There is no way by which we can duck the responsibility for being right in our conclusions and our advice. Such work as this, therefore, is not an academic exercise, but a serious act of judgment in the avoidance of a risk. One may take the point of view that the use of such products is an expression of human vanity, and, as such, entirely unnecessary. Such may be the case. I do not set myself up as an authority in such matters. I only feel strongly the right of a human being to make his own choices in such matters, provided he knows the extent of his risk and the need to take suitable precautions against the possible hazard. Moreover, the effort to meet his wishes in this and a thousand and one other matters, cannot, I think, be regarded as a reprehensible, or even an insignificant feature of national commerce.

But so much for the philosophy of life and action. My opinion in this matter, from all of the consideration which I have given it, including the test of experimentation with human beings, is that there is no hazard which is not easily avoided by simple precautions well within the expectation of persons who are more than ordinarily interested in themselves, as indicated by the very nature of their willingness to use this product. The hazard is not intrinsic in the product, but resides in the performance of the individual in avoiding the unnecessary ingestion of the product as it is applied and is available in modest quantity on the surface of the hair, where it may contaminate the fingers of the user.

Now as to the information which I agreed to supply. I read carefully the article by Hine et al., and I believe that their experiments were conducted properly, and I would be inclined to accept the validity of their conclusions, from their work. My only

criticism of any moment lies in their failure to investigate pure compounds as well as the mixtures. We need to know, I think, the behavior of pure compounds as applied upon the skin. I strongly suspect that we dare not generalize, at present, with safety, in these matters, for the compounds will behave differently, as to their rates of absorption dependent upon their individual properties, and then will be influenced somewhat by the vehicle or mixture of solvents or emulsifying agents in which they are dealt with.

However, despite our consideration of all of these matters, those experiments are not strictly relevant to the issue of the type of hair dye being considered. Indirect information does not answer the questions which arise in one's mind concerning these hair dyes. For this reason, one had to test the specific type of materials concerned. If one had to judge this situation on such evidence as that conveyed by the experiments of Hine et al., we would indeed be in a quandary. These experiments were carried out to test certain other materials which are being used in an entirely different manner. They provide certain answers to the questions raised about these commercial products, and they have served this purpose alone.

I did not think that any other means existed for deciding the issue of the hazard of the percutaneous absorption of lead from these hair dyes, in the course of their use, than that of making use of a characteristic material in a more severe manner than that specified in their normal use, and seeking to determine the extent of the absorption of lead during the process. Incidentally, the long-term experiments which we have carried out on a number (20) of human subjects over long periods of time (months and years up to four of the latter) have yielded the best information available as to the behavior of lead in the human body. There is simply nothing comparable to these experiments in the literature of the world on lead. They have answered questions which otherwise have remained unanswered for a very long time, and they have done so only because I would not accept the responsibility for the safety of people who were to work with lead, until I had the means of answering some of those questions. Since the money required to conduct such experiments was made available to me and my associates, we were enabled to conduct them. It is now known, for example, that the most sensitive means of detecting the absorption of lead by the intact, healthy human being, is that of finding a significant elevation of the rate of his urinary excretion of lead. By "significant" is meant that the increase in the rate of excretion cannot be explained by the absorption of lead from any other source than that being tested; and that the increase is of such proportions as to be "actual" rather than "apparent," in terms of analytical deviations. The other "sources" which must be controlled are the ordinary environmental sources (which must be thoroughly investigated or controlled during the experiments).

In the matter of the toxicity of lead, as indicated by the L.D. 50 of soluble salts of lead administered orally to experimental animals, let me say at the outset that information of this type is utterly irrelevant to the hazard, if any, associated with the use of these hair dyes. The issue here is that of the significance of a contribution - some contribution, however small - to the absorption of lead which derives, otherwise, from the lead in food and beverages consumed regularly and from that in the ambient air - that is, lead currently present in the environment of man. The extent of the absorption of lead from the environment is now known fairly well, with respect to that of large segments of the population of the United States. This has been going on for centuries (with appreciable increase in the past three or four decades), and the question arises, of course, as to how far this increase can go without offering a threat to the general population, including certain segments of it which are more severely involved than the others. The Food and Drug Administration is responsible

for preventing further increases in food, beverages, cosmetics, therapeutic agents, etc., and this responsibility must be recognized as an essential feature (along with the observations of other professional investigators and observers of the current scene) of public health.

The actual data as to the toxicity of the soluble salts of lead administered orally to experimental animals are few and far between, since for the most part, investigators have been very much more interested in the effects of intravenous, intraperitoneal and subcutaneous administration of lead, except when the prolonged administration of sublethal quantities was desired. Nevertheless, there is information.

A Handbook of Toxicology, edited by William S. Spector was issued in 1956, by the Division of Biology and Agriculture of the National Academy of Sciences and The National Research Council. It was published by W.B. Saunders Company, Philadelphia and London, and is one source. The following data (among many others) are given. (I think there are others since, but I have not undertaken to find them.)

Lead Acetate lethal to the dog in the dose of 300 mg. per kg. in 11 days. Flury, Abderhalden's Handbook 4-7B:1314.

Lead Chloride The minimum lethal oral dose for the guinea pig is 1500-2000 mg. per kg., according to Tartler, Arch. Hyg. 125:273, 1941.

Lead Lactate The L.D. 25, for the guinea pig, according to Tartler (same reference as above), is 1000-4000 mg. per kg.

Lead Nitrate The lethal dose, for the guinea pig, according to Tartler (same reference as above), is 2000 mg. per kg.

As for the man mentioned in our report for continuing observation in association with his continuing use of the hair eye, he gave up the use of the material after a very few more applications than those reported in the report. (He is in the maintenance group of the various workmen for Kettering Laboratory and the building which houses the laboratories and offices of Anatomy, Biochemistry, Physiology, Pharmacology, Medical Arts and Preventive Medicine - of the Medical College of this University. He was originally one of the members of the maintenance staff of the Kettering Laboratory alone, and was employed in the first instance by me when I was Director of the Kettering Laboratory. In any case, he is well known to me as a thoroughly reliable person.) This man, Francis Sullivan, by name, is not a vain man at all, and after a few applications, he found the use of the material too much of a nuisance to continue. No further reason for continuing observation exists.

I believe this covers the matters about which we talked in Washington, D.C. last Thursday. If I have omitted anything of importance, please do not hesitate to let me know. Also, if anything else comes to your mind on which you need, or wish, to consult me, let me know. Moreover, if the people in F.D.A. wish to talk with me further, I shall be available at some mutually convenient time. This, of course, is up to them. I would not invite myself to talk to them, on any account.

Cordially yours,

Robert A. Kehoe, M.D.
Professor Emeritus of
Occupational Medicine

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P.S. I return herewith the reprint that you let me have. RAK