Solubility and the Relative Toxicity of Lead Chromate II

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IN A PREVIOUS study,[1] we provided evidence that lead chromate inhaled or ingested by human subjects did not exhibit clinical or laboratory findings indicative of lead absorption after exposure to quantities of lead chromate greatly in excess of those regarded as safe for continuous exposure. That study involving two groups of 145 men and 40 men for 16 months was extended to 28 months for 20 men who were still exposed to high concentrations based on an exposure day.

We will, in this report, extend the observations to 40 months for 26 men. The information is evaluated in terms of the solubility relations of lead salts in human lung fluids.[2]

I. Exposure to $PbCrO_4$

IN OUR previous report on the toxicity of lead chromate,[1] we evaluated the actual exposure of two groups totaling 185 men to amounts of lead in the form of lead chromate, never less than 4.0 mg. of $PbCrO_4$ per exposure day for 18 months, and to over 18 mg. $PbCrO_4$ per exposure day for from 12 to 15 months, with no clinical or laboratory symptoms of lead absorption. From the above group, 26 men were selected on the basis of continuous exposure to the highest concentrations of lead chromate. They had exposure days averaging 6.2 mg. of Pb chromate for 27 additional months. The reports showed no laboratory or clinical results differing from the normal.

This group of 26 men had exposure days of over 18.3 mg. lead chromate per day for 13 months, and to 6.2 mg. lead chromate per day for 27 additional months. The highest exposure day was 12.2 mg. and the lowest was 2.6 mg. in this 27-month period. The men on the job cooperated by wearing the test collecting devices. At the end of 40 months, the group Basophilic Aggregation was .7 and the lead-in-urine average .039 mg. per liter. Again, no clinical or laboratory results deviating from the normal were found.

The above extension of the test results of the group, whose only selection was on a basis of continuous exposure to high quantities of lead chromate, indicates that over long periods of time, such exposure does not cause demonstrable ill effects.

In view of Silverman and Drinker's[3] questions about physiological breathing rates, our last results for a period of 15 months with this group of 26 men were derived mainly from the exposure days of the men on the job. All the men cooperated to some extent, and no significant deviations were noted from those results which had previously been extended from a limited number of men. These tests were not taken every day, but some values were obtained every two weeks from different individuals. The individual differences which did appear were not important to the general average over a long period of time. The actual exposure time of no worker was reduced for more than two weeks over the total exposure time by the wearing of test equipment.

Efficiency of Packed Tube Collector

THE efficiency of the "packed tube collector"[1] was checked at 28 and 40 liters airflow per minute using an electrical precipitator in a series. Three determinations averaged 99.7% relative efficiency at 28 liters per minute, and three determinations at 40 liters airflow averaged 99.8% relative efficiency. The lead test material was sprayed lead chromate in concentrations of 120 to 150 milligrams of lead chromate per 10 cubic meters of air as determined by the electrical precipitator.

Air Lead Concentrations per Ten Cubic Meters

HOWEVER, the concentrations that this group of 26 men were exposed to based on the amounts of lead chromate per 10 cubic meters of air using the electrical precipitator and the midget impinger as sampling equipment were much higher. The averages comprise 328 individual air tests for the first 13-month period, and 628 separate air determinations for the 27-month period. For 13 months, the exposure average was 117.1 mg. of lead chromate for 10 cubic meters of air. For the following 27 months, the average was 41.3 mg. of lead chromate per 10 cubic meters of air. The lowest values found in one area where two of the men were working averaged 12.1 mg. of lead chromate per 10 cubic meters of air for the last six months' exposure period.

An outside agency checking one of the work places where some of these 26 men had worked for over 15 months reported lead-in-air values of 74, 105, 118 and 121 mg. of lead per 10 cubic meters of air using the electrical precipitator as the collecting instrument.

Since such methods of standards reporting, based on the air content of contaminant per 10 cubic meters of air, are commonly employed, it can be seen that some explanation is required as it is determinable that lead absorption of lead compounds such as lead oxide, when reported in much smaller concentrations, has caused lead absorption.

Thus, our correlations[4] between lead-in-urine and Basophilic Aggregation were good when lead oxide was involved. Furthermore, our first lead chromate report[1] cites the excellent agreement between Basophilic Aggregation, lead-in-urine, and lead content of the air when coarse *lead oxide*

is involved. We have additional information supporting this point. Two hundred and one (201) men exposed to concentrations of lead-in-air averaging 1.24 mg. of lead per 10 cubic meters had a Basophilic Aggregation average of .9, and the lead-in-urine average was .081 mg. per liter of urine.

Other investigators[5,6] have somewhat similar data which refer in the main to soluble lead compounds—compounds readily soluble in bodily fluids.

We have found that when lead chromate[1] was involved, this correlation was not evident. There is a correlation between the Basophilic Aggregation and the lead-in-urine, but none with the amounts of lead-in-air.

Hypothesis

OUR WORK[2] on the solubility of lead salts in human pleural fluid shows that lead oxide and lead carbonate are much more readily soluble in human lung fluid than lead chromate and lead titanate. This fact, when isolated from the actual concentrations, is only important in that it allows a prediction that the more soluble salt will probably cause signs of lead absorption to appear more rapidly than in the case of the less soluble salts.

However, we believe the quantitative evaluation of the amounts of impure lead chromate in human pleural fluid[2] indicates a possible explanation of the lack of harm due to very large quantities of inhaled lead chromate. It has been suggested that the synthetic coating on the lead chromate paint would prevent the dissolving of the lead compound in the human organism, but this is not a noticeable deterrent to lead intoxication when paints containing lead oxide, lead sulphate, or even lead carbonate are sprayed.

Furthermore, we did *not* use a coated lead chromate in our solubility determination.

These quantities had not been reported in the literature for the solubility of the lead oxide, lead carbonate, lead chromate, and lead titanate in human pleural fluid or blood serum prior to our recent paper.[2] We are now suggesting a possible explanation which has been offered freely in the past based on generalized information or belief. We now have scientific data to substantiate these beliefs.

We propose an explanation based on the extremely low solubility of lead chromate in human pleural fluid and blood serum. The amounts found soluble in one liter of these fluids range from 1.28 mg. $PbCrO_4$ in pleural fluid to 1.14 mg. $PbCrO_4$ in blood serum. Since the total amount of tissue fluid which could act as an exchange medium between the lung and the blood is limited, a saturation of this limited quantity of fluid would provide total quantities of lead ion less than 1.0 mg. This quantity of lead is subject to a continuous unbalanced equilibrium with the blood, and finally with the kidney and the excretory product, the urine. The maintenance of saturation of these fluids would require, according to the laws of mass action, very large quantities of the less soluble lead chromate in the lung. When it is considered that usually, but not always, no clinical symptoms are observed when .2 to .3 mg. of lead are found in a liter of the urine and amounts of .05 to .1 mg. of lead per 100 grams of whole blood, the possibilities of getting even .5 of a milligram of lead in the body fluids from a quantity of lead chromate of 1.0 mg. per liter of body fluid concentration is remote in even exceptional industrial exposures.

This information may appear more significant if we point out that .05 mg. to .1 mg. of lead per 100 grams of whole blood is close to .5 to 1.0 mg. of lead *per liter* of blood. We, therefore, are comparing .2 to .3 mg. lead in the excretory product, the urine, to .5 to 1. mg. of blood lead in the same volumes of fluids to a compound which dissolves in blood serum in the range of 1.14 mg. per liter.

Actually, our measurements of 26 men exposed to at least 6.2 mg. of lead chromate for over 40 months, and for a large portion of the time to from 15 to 20 mg. per day, showed that this saturation was not only not reached, but that the lead-in-urine and Basophilic Aggregation dropped to normal during a period of time when the exposure day indicated an inhalation of 6.2 mg. of lead chromate. Furthermore, for 13 months of exposure to over 18 milligrams of lead chromate, no significant deviations were noted from the results observed at the end of one month's exposure.

Based on these observations, we suggest that the insoluble lead salts which prove to have solubilities in the range of 1 milligram or less in human lung fluid at about 37° C will not be likely to be causative of lead intoxication from inhalation in quantities of less than 20 milligrams of insoluble lead compound per 10 cubic meters of air. We do not propose this as a standard of the M.A.C. variety, but we do suggest that it is a fact based on scientific observation.

It is our observation that even this figure may be extended considerably if more insoluble lead salts are considered. Thus, with purified lead titanate where the solubility is about .28 mg. $PbTiO_3$ per liter of blood serum, we may be approaching a range where a true equilibrium exists between the amounts of lead absorbable through inhalation and the amounts excreted without harm to the human organism. This relation would not obtain with impure lead titanate containing lead salts readily soluble in body fluids. It is believed that any lead intoxications which may occur in a lead salt of this level of solubility would be due to the admixture, or formation of a more soluble lead compound.

Solubility, Particle Size and Excretory Rates

OUR STUDY of workers exposed to lead chromate[1] has led to the question as to whether or not somewhat higher levels of urinary excretion than that of the general population can be maintained without the demonstration of clinical symptoms.

In the cases of over 100 men exposed to large quantities of lead chromate, the urinary lead excretory rate rose to .1 mg. per liter of urine and remained above .06 mg. per liter of urine for 18 months with no demonstrable damage. Certainly there must be some regulatory mechanism to adapt the organism to changed conditions. In a previous study,[4] we were able to show that the average individual in an industrial environment, exposed to more lead than the normal population, *did* have a somewhat higher lead excretory rate of .05 mg. per liter of urine than had been reported for the general population.[7] This indication has been supported by Dreessen[8] in his study on lead storage battery workers not exposed industrially to lead, whose urine contained .06 mg. of lead per liter.

That this rate is in equilibrium with the exposure is shown by the return to completely normal industrial levels, both for lead-in-urine and for Basophilic Aggregation test, even though exposed to over 6 mg. of lead chromate when in the air of the work place, and over a longer period of time, the lead-in-urine concentration and Basophilic Aggregation percentage approach the normal values given for the general population.

Summary and Conclusion

WE DO NOT conclude that lead chromate cannot cause lead poisoning under certain conditions, but the evidence we have presented makes the appearance of lead intoxication from this source highly improbable in the industrial exposures which are likely to be encountered. This conclusion is based almost entirely on the solubility characteristics of this compound. In those instances where the amounts of lead compounds which can be dissolved in body fluids, are equal to, or less than, the amounts which are transported and eliminated without harm to the organism, the potential saturation limit is the important factor. The factor of solubility, in this instance, is independent of particle size and, perhaps, of other possible influencing factors, whereas lead compounds soluble to a great degree in body fluids are dependent on particle size, both in regard to the rate of solution and other factors such as the transport of extremely fine particles in protecting envelopes.

References

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"It Is The Nurse . . . ."

A SICK workman is a piece of humanity broken into bits. The physician picks up one to study it under his stethoscope, the bacteriologist wants another for his microscope, the psychologist a third one and so on. And each of them brings his own particular knowledge to bear on the particular bit, and draws particular inferences from it, sometimes right, sometimes wrong. But in the end it is the nurse who gathers up the various bits and reconstructs a whole from them with the virtue of her motherhood and the alchemy of her smile. While scientists keep busy sharpening their intellects in this or that particular direction the nurse enlarges her heart to include in it the whole of humanity. MCGRATH has said in her book "Nursing in Commerce and Industry" that industry needs a superior nurse. It is better if she had used the word religious in place of superior, for only such a nurse as lives religion in her life can be a superior one.

—From "Industrial Medicine: Its Religious Aspect," by H. P. DASTUR., Medical Officer, Industrial Medical Department, Tata Industries, Ltd., Bombay. In *J. Indian Med. A.*, 13:3, 279-281, May, 1940.