

THE SOLUBILITY OF LEAD SALTS IN HUMAN
GASTRIC JUICE, AND ITS BEARING ON
THE HYGIENE OF THE LEAD IN-
DUSTRIES *

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The following investigation was undertaken at the request of Dr. Alice Hamilton, special investigator of lead-poisoning for the federal Bureau of Labor, because of the availability in our laboratory of normal human gastric juice.

The relative importance of the skin, the lungs, and the digestive tract as avenues of the lead absorption in workers in the lead industries seems to be determined only to this extent that the skin is the least important. While lead may be absorbed through the intact skin under special conditions of prolonged application of lead compounds to the skin, it may be questioned whether under ordinary working conditions absorption through the skin contributes to industrial plumbism. There remains, then, to consider the lungs and the digestive tract. Meillère¹ seems to show that while poisoning may occur by absorption of lead from the lungs, this is not a channel of absorption of practical importance in the industries. Goadby,² on the other hand, concludes that absorption from the lungs is the prime factor in most forms of plumbism. Goadby subjected cats to breathing air charged with various kinds of lead dusts. Lead-poisoning resulted in every case. The only precaution taken against lead dust reaching the stomach was brushing as much of the lead dust as possible from the animals' fur at the end of every inhalation period. It is therefore certain that some of the lead dust was swallowed with the saliva and the mucus from the respiratory passages. But Goadby's experiments seem to show that when the same lead dusts are given by mouth a much greater quantity is required than in the case of inhalation, the ratio estimated being 100:1. Thus, one cat (No. 12) was fed 0.8 gm. dry white lead a day for eighteen months without producing any other symptoms than some loss of weight. Other cats fed similar quantities of white lead daily developed symptoms only when alcohol was administered at the same time. This extraordinary tolerance of cats to dry white lead by mouth cannot be accepted as normal, in view of the results of our own feeding tests with white lead to dogs and cats. Legge and Goadby² point out that, on the whole, cases of lead-poisoning are most frequent in the industries in which the lead dusts are not adequately controlled. This is unquestionably true, but it does not follow that this lead dust enters the body mainly, or at all, by the lungs.

The lead dust, like any other dust, settles all over the person exposed to it. It permeates his clothes, and settles on the skin, the hair, in the mouth and in the respiratory passages. In the mouth the dust acts as a stimulus to salivation, and in an animal like the cat, which does not expectorate, this increases the frequency

of swallowing. Some men are in the habit of swallowing the mucus from the trachea—and even that from the nasal passages. It is, therefore, obvious that the chances for swallowing lead increases greatly with the presence of lead dust. At the same time some of the lead dust particles must reach the alveoli of the lungs, and may pass into the body without solution like particles of carbon. But most of the lead dust that penetrates down to the bronchioles and alveoli must, unless dissolved, become entangled in the film of mucus and eventually be passed out by way of the trachea. It is well known that after breathing coal dust or dense smoke for an hour a man may continue to discharge carbon-stained mucus from the trachea for more than twenty-four hours. It is obvious that only an insignificant fraction of the insoluble dust in the respired air is taken up by the alveolar cells, or by the leukocytes and retained by the lymph-nodes. The carbon particles in the lungs and lymph-nodes of an old coal-miner or a stoker probably amounts to less than a gram, while the quantity of carbon passed in and out of the lungs by way of the trachea must have reached many kilos.

Lead-poisoning occurs in industries in which no lead dusts are produced. And since lead dust in the respired air increases the chances of lead dust entering the stomach, it is clear that the digestive tract is in some cases the sole, and probably in all cases, the most important avenue of absorption of the lead in industrial lead-poisoning.

There is no evidence that the lead salts are absorbed from the digestive tract or act locally on the mucosa, except when in solution. The strongest solvent in the digestive tract for the lead salts is the hydrochloric acid of the gastric juice, and of less importance the lactic acid, and other organic acids produced in the course of hydrolysis of proteins and of fats and of bacterial activity. In view of the humane and economic importance of lead-poisoning in the industries, the literature on the action of the gastric juice on the different lead salts appears fragmentary. It was even assumed until recently that lead sulphate is practically insoluble in the stomach and intestines. This view led to the practice of giving sulphuric acid lemonade to lead workers as a prophylactic measure. Blum,³ Goadby,⁴ Schicksal⁵ and Beck⁶ have studied the solubility of various lead salts in dilute hydrochloric acid, in various artificial gastric digest mixtures, and in gastric juice. All agree that the lead sulphate is soluble in these mediums. One of Goadby's two experiments with human gastric juice (10 c.c. gastric juice plus 0.1 gm. of the lead salts, at 37 C. [98.6 F.], for one hour) appears to show that the lead sulphate is more soluble than is lead carbonate (white lead) or lead oxid (litharge). The second experiment showed practically the same solubility for the three salts. The work of Blum and Schicksal indicates that the presence of peptone in gastric digest mixtures increases slightly the solubility of the lead salts.

MATERIAL

Samples of paint dust of basic lead carbonate and basic lead sulphate, respectively, were sent us by Mr. A. M. Johnson, chief chemist of the Pullman Company. Mr. Johnson stated that the samples submitted were typical of the paint dust produced in the Pullman shops

* Read in the Section on Pharmacology and Therapeutics of the American Medical Association, at the Sixty-Fourth Annual Session, held at Minneapolis, June, 1913.

* From the Hull Physiological Laboratory of the University of Chicago.

1. Meillère: *Le Sâturnisme*, Paris, 1903.

2. Goadby: *Jour. Hyg., Cambridge*, 1909, ix, 122. Goadby and Goodbody, *Lancet*, London, 1909, ii, 988. Legge and Goadby, *Lead-Poisoning and Lead Absorption*, London, 1912.

3. Blum: *Wien. med. Wchnschr.*, 1904, lii, 538; *Deutsch. med. Wchnschr.*, 1912, xxxviii, 645.

4. Goadby: *Jour. Hyg., Cambridge*, 1909, ix, 122.

5. Schicksal: *Die Bekämpfung der Bleigefahr in der Industrie*, 1908.

6. Beck: *Arch. a. d. k. Gesundheitsamte*, 1910, xxxiv, 446.

by sandpapering painted metal. The dust samples contained, per gram, lead corresponding to the following quantities of lead sulphate: basic lead carbonate paint dust, 1.04, 1.04 and 1.06 gm., respectively, 1.05 gm. average of three samples; basic lead sulphate paint dust, 0.86, 0.87 and 0.82 gm., respectively, 0.85 gm. average of three samples.

Samples of sublimed white lead (basic lead sulphate) and of lead carbonate ("Old Dutch Process") were sent us by the Pilcher Lead Company, Joplin, Mo. These samples were not mixed with oil. On analysis they were found to yield per gram the following quantities of lead sulphate: lead carbonate, two samples, 1.12 gm. each; basic lead sulphate, two samples, 0.98 and 0.96 gm., respectively, 0.97 average.

Normal human gastric juice was obtained from a man 27 years old, with complete constriction of the esophagus and a gastric fistula of sixteen years' standing.⁷ The juice was secreted while the man was chewing palatable food when hungry. Hence it was normal "appetite" or "psychic" juice, not mixed with saliva. The total acidity varied from 0.40 per cent. to 0.52 per cent.

I. THE RELATIVE SOLUBILITY OF LEAD CARBONATE AND LEAD SULPHATE (PAINT DUSTS AND PURE SALTS) IN GASTRIC JUICE

The results are given in Tables 1 to 4. The lead carbonate proved in every case to be much more soluble than the lead sulphate. The lead carbonate paint dust is nearly as soluble as the pure white lead, while the lead sulphate paint dust is less soluble than the pure basic lead sulphate. We are at a loss to account for Goadby's results showing greater solubility of the lead sulphate in gastric juice, except on the hypothesis of faulty methods. A greater solubility of lead sulphate than of lead carbonate in gastric juice seems a chemical impossibility. We note that Goadby records only two tests and the lead was determined after centrifuging the digestive mixture instead of in clear filtrate. It seems probable that varying quantities of the lead salts were present in suspension in addition to that which was present in actual solution.

Peptone in concentrations of 0.2 per cent. and of 1 per cent. does not have any marked influence on the solubility of the lead salts, but the influence of peptone, so far as it is in evidence, is in the direction of increasing the quantity of lead dissolved. The formation of lead peptone compounds might lead to the setting free of the chlorin ions in the lead chlorid, and thus to the formation of more lead chlorid from the carbonate and the sulphate. Our figures show that this is not an important factor in lead-poisoning from the digestive tract.

The solubility of the lead salts in pure gastric juice is practically the same as that in similar quantities of 0.5 per cent. hydrochloric acid. It is therefore clear that the hydrochloric acid of the gastric juice is the all-important solvent. Pepsin, rennin, and other organic constituents may combine with the lead salts when in solution, but if this is the case the reaction does not appreciably affect the quantity of lead salts held in solution.

We were especially interested in the action of milk on the solubility of the lead salts in human gastric juice and weak solutions of hydrochloric acid, in view of the fact that in some places lead workers are required to drink milk before starting work. And practical experi-

ence seems to show that milk or other food in the stomach minimizes the danger of lead-poisoning from the digestive tract. When milk and gastric juice are mixed in the proportion of one to one, lead salts added and the mixture incubated at body temperature for ten hours, not enough lead goes into solution to give a qualitative lead test. In two cases a positive qualitative test was obtained when the lead carbonate paint dust was used. The same results are obtained in mixtures of milk and 0.05 per cent. hydrochloric acid. But when the ratio of the gastric juice or hydrochloric acid to the milk is increased the lead salts are dissolved in proportion to the increase in the quantity of gastric juice or hydrochloric acid (Table 4).

The foregoing action of milk is probably due to the fixation of the hydrochloric acid by the milk proteins and the neutralization of the hydrochloric acid by the carbonate of the milk. Hence, when an excess of milk is added to the gastric juice there will be no hydrochloric acid to effect solution of the lead salts, while in the presence of an excess of gastric juice some free hydrochloric acid remains to act on the lead. We are inclined to the view that the formation of insoluble lead albuminates is a factor of minor importance in the above-mentioned action of milk.

These experiments *in vitro* do not reproduce some of the conditions that obtain in normal gastric digestion. The fixation of the hydrochloric acid by the proteins takes place in the stomach as well as in the test-tube, so that the presence of proteins retards the appearance of free hydrochloric acid in the contents of the stomach. But the work of Cannon and others renders it highly probable that relaxation of the pyloric sphincter and entrance of the gastric content into the duodenum is ordinarily preceded by the development of some free hydrochloric acid in the pyloric portion of the stomach. This hydrochloric acid will, of course, tend to dissolve any lead salts in the chyme until it is neutralized in the duodenum. Albuminous foodstuffs can therefore diminish the solution of lead salts in the stomach only to the extent that they fix the hydrochloric acid in the gastric juice.

The taking of milk is a more efficient prophylactic measure than the taking of an equal amount of other forms of proteins, because there is less appetite secretion of gastric juice with milk, and the fat in the milk depresses and retards the action of gastric secretagogues.

II. THE ACTION OF BILE ON THE LEAD SALTS

The ferments of the pancreatic juice and the intestinal juice have, of course, no action on the lead salts, except indirectly in case of lead albuminates and similar combinations, formed in the stomach by lead salts already in solution. The solution of lead salts in the intestines must therefore depend on the weak organic acids produced in the hydrolysis of the foods, or bacterial action, and on the alkalinity of the digestive juices poured into the intestine.

Normal pancreatic juice was not available to us, but a number of tests were made of the possible solution of the lead sulphate and the lead carbonate paint dust in dog-bile and ox-bile. When mixed in the following proportion, 25 c.c. bile plus 25 c.c. water plus 0.5 gm. of the lead salt, with or without peptone, at 38 C. (100.4 F.), for ten hours, not enough of lead went into solution to give a qualitative test for lead. This applies to both the carbonate and the sulphate paint dusts. The presence of peptone had no effect.

⁷ Carlson, A. J.: Am. Jour. Physiol., 1912, xxxi, 151.

III. THE RELATIVE TOXICITY OF BASIC LEAD SULPHATE
AND BASIC LEAD CARBONATE (PAINT DUSTS AND
PURE SALTS) WHEN FED TO DOGS AND CATS

Since it is not possible in experiments *in vitro*, even when normal gastric juice is available, to reproduce some of the essential conditions of gastric digestion, the final solution of the question of the relative toxicity of the different lead salts must be sought by feeding experiments. Goadby fed various lead salts to cats. Five cats received from 0.5 gm. to 0.8 gm. dry white lead (lead carbonate) per day for periods varying from one to eighteen months. According to Goadby this quantity of lead carbonate per day produced practically no symptoms unless alcohol was given at the same time. One must infer from Goadby's work that cats are unusually resistant to lead salts given by mouth. In an earlier work Leymann⁸ showed, however, that even the slightly soluble lead sulphate produces toxic symptoms in eight or nine days when fed to cats in quantities of 0.2 gm. per day. Blum⁹ concludes that the sulphate is less toxic than the other lead salts employed in the industries.

FEEDING EXPERIMENTS (SERIES I)

Dogs of nearly the same size and age were selected, and 4 gm. of the lead sulphate and the lead carbonate paint dusts respectively were fed to the dogs in ground meat, either in one feeding or in two feedings, eight hours apart. The results are summarized in Table 5.

The feces of Dogs A and B (Table 5) were collected for six days after giving the lead paint dust per mouth, and the quantity of lead determined, with the following result:

Dog B, fed 4 gm. basic lead carbonate, containing 4.16 gm. lead determined as sulphate. Lead recovered in the feces, 2.61 gm. or 62 per cent.

Dog A, fed 4 gm. basic lead sulphate, containing 3.28 gm. lead determined as sulphate. Lead recovered in feces, 3.10 gm. or 94 per cent.

The lead in the feces of Dogs C and D was not determined.

FEEDING EXPERIMENTS (SERIES II)

Eight dogs were selected for this test, and grouped in pairs of approximately the same body-weight. One of the dogs of each pair was fed the sulphate paint dust in meat, the other one given the carbonate paint dust in meat. The quantity of the lead paint dusts given each dog was fixed to equal 0.1 gm. lead sulphate per kilo body weight. The dogs fed the sulphate paint dust thus received a greater quantity of the dust, as this dust contained a lower percentage of lead than the carbonate paint dust.

The results are summarized in Table 6. The table shows that the dogs receiving the lead carbonate paint dust developed severe symptoms of acute lead poisoning within from twenty-four to forty-eight hours after the first feeding, while the dogs fed the sulphate paint dust showed very mild symptoms of lead intoxication only after three or four feedings, that is, after from seventy-two to ninety-six hours. Feeding experiments as tests of relative toxicity break down, of course, as soon as vomiting or lack of appetite appears, as one cannot control the quantity of lead salts eaten or retained. For that reason the experiment was discontinued as soon as there appeared symptoms of intoxication in the dogs receiving the least toxic lead salt, that is, the sulphate.

FEEDING EXPERIMENT (SERIES III)

The results of the feeding tests with the sulphate and the carbonate of lead to dogs do not agree with those of Goadby on cats. It does not seem likely that cats have so much greater tolerance than dogs to lead salts by mouth. Legge and Goadby claim, indeed, that cats are especially susceptible to lead-poisoning. Moreover, Leymann obtained symptoms in cats from feeding 0.2 gm. lead sulphate per day

for eight to nine days. How are Leymann's results on cats and our results on dogs to be reconciled with Goadby failing to produce lead-poisoning in cats on feeding the more toxic lead carbonate in daily doses up to 0.8 gm. for two to eighteen months? It is difficult to understand where any material source of error might be concealed in the relatively simple process of mixing lead salts with the food and observing the animals.

Our own test series consisted of four healthy cats, which we may designate as A, B, C and D. The quantity of the lead salts mixed with the food each day was fixed to equal 0.1 gm. of lead sulphate per kilo body weight of cat. The amount of ground meat, fish or milk and bread with which the lead salts were mixed was less than each cat would ordinarily eat per day, so as to insure all of the lead salts reaching the stomach.

Cat A.—Fed 0.3 gm. lead carbonate per day. The first three days the cat did not touch the food, although a new lot was prepared each morning. On the fourth day the cat ate about four-fifths of the food. No symptoms were observed, but the cat did not touch the food for two days following. On the seventh to the eleventh day the cat ate about one-fourth of the food each day. No obvious symptoms of lead-poisoning.

Cat B.—Fed 0.37 gm. lead sulphate per day. Cat refused the food-lead mixture the first three days. The fourth day the cat ate all the food; on the sixth to the eighth day about one-third of the food. On the ninth day all the food was consumed, but on the two following days less than half of it was taken. No lead intoxication in evidence.

Cat C.—Fed 0.31 gm. basic lead carbonate paint dust per day. First day cat ate about three-fourths of the food-lead mixture; second day cat ate about half of the mixture. On the morning of the third day the cat had vomited a considerable mass of partly digested meat. The cat seemed depressed during the third to the eighth days and refused all food. During the ninth to the eleventh days the cat ate about one-fourth of the food each day. There were no further symptoms.

Cat D.—Fed 0.3 gm. basic lead sulphate paint dust per day. The cat did not touch the food-lead mixture during the first three days. On the remaining eight days of the feeding period the cat ate all the food on four days and on the other days about one-third of the food. No symptoms of lead-poisoning appeared at any time.

This eleven-day feeding period convinced us of one thing only, namely, that mixing the lead salts with the food is not a feasible method in the case of cats. Through taste or odor the addition of these small quantities of lead salts to the ground meat, fish or milk and bread renders the food mass so unpalatable that the cats will starve for days rather than eat, and one cannot be certain of the cat eating even a small portion of the food on any day. In a test of the relative toxicity of the two salts it is, of course, essential that all of the salts given shall reach the stomach each day. The method of mixing the lead salts with the food was therefore abandoned. A second series of four cats was selected and 0.1 gm. of the lead salts per kilo body-weight was administered in gelatin capsules each morning before giving the customary food. The results are given in Table 7.

The cats varied in weight from 2.5 kg. to 3.5 kg. Hence 0.25 gm. constituted the smallest and 0.35 gm. the largest dose of lead salts given per day. Toxic symptoms were produced by all the salts, but the lead carbonate and the lead carbonate paint dust were distinctly more toxic than the basic lead sulphate and the lead sulphate paint dust. The toxic symptoms noted were vomiting, loss of appetite, constipation and depression. The feeding period was too short for the development of the chronic nervous symptoms.

It will thus be seen that cats and dogs show about the same susceptibility to lead intoxication by mouth. Lead carbonate and lead sulphate when given daily in quantities up to 0.1 gm. per kilo body weight produce toxic symptoms within two to eight days.

8. Leymann: Arch. f. Hyg., 1892, xvi, 316.

9. Blum: Deutsch. med. Wchnschr., 1912, xxxviii, 045.

IV. SUMMARY

1. *Solubility of White Leads in Human Gastric Juice*

WHITE LEAD PAINT DUSTS

Solubility in pure gastric juice (25 c.c. juice to 0.5 gm. lead):

Basic lead carbonate paint dust, 46%.

Basic lead sulphate paint dust, 5.7%.

Solubility in gastric juice + peptone (25 c.c. juice, 0.1 gm. peptone, 0.5 gm. lead):

Basic lead carbonate paint dust, 46%.

Basic lead sulphate paint dust, 7.3%.

Solubility in gastric juice + milk (juice 1 : milk 1):

Basic lead carbonate paint dust, none = 0%.

Basic lead sulphate paint dust, none = 0%.

Solubility in 0.5% HCl (25 c.c. HCl to 0.5 gm. lead):

Basic lead carbonate paint dust, 66%.

Basic lead sulphate paint dust, 6.7%.

Solubility in 0.5% HCl + milk (HCl 1 : milk 1):

Basic lead carbonate paint dust, none = 0%.

Basic lead sulphate paint dust, none = 0%.

Solubility in 0.5% HCl + milk (HCl 2 : milk 1):

Basic lead carbonate paint dust, 25.4%.

Basic lead sulphate paint dust, 1.5%.

Solubility in 0.5% HCl + milk (HCl 4 : milk 1):

Basic lead carbonate paint dust, 83.5%.

Basic lead sulphate paint dust, 6.9%.

WHITE LEADS

Solubility in pure gastric juice (25 c.c. juice to 0.5 gm. lead):

Lead carbonate ("Old Dutch Process"), 53%.

Basic lead sulphate 25%.

Solubility in gastric juice + peptone (25 c.c. juice to 0.5 gm. lead):

Lead carbonate ("Old Dutch Process"), 57%.

Basic lead sulphate, 27%.

Solubility in pure gastric juice (50 c.c. juice to 0.5 gm. lead):

Lead carbonate ("Old Dutch Process"), 69%.

Basic lead sulphate, 30%.

Solubility in gastric juice + milk (juice 4 : milk 1):

Basic lead carbonate, 90.0%.

Basic lead sulphate, 34.8%.

2. *Toxicity of White Leads When Fed to Dogs and Cats*

The lead carbonate is much more toxic than the lead sulphate. But both salts produce acute lead poisoning when given in quantities of 0.1 gm. per kilo body-weight daily.

3. *The Influence of Milk*

When milk and gastric juice are mixed in the proportion of 1:1, the hydrochloric acid of the gastric juice is so completely fixed by the milk proteins or neutralized by the carbonates in the milk that the mixture has virtually no solvent action on the lead salts; but when gastric juice is present in excess the lead salts go into solution in proportion to the excess of the gastric juice. When milk is taken into the stomach there occurs, of course, a similar fixation of the hydrochloric acid, and, in addition, the total quantity of gastric juice is diminished owing to the inhibitory action of the fats in the milk on the processes of secretion.

4. *Practical Suggestions*

On the basis of our work we venture to offer these two practical suggestions:

1. The lead carbonate is so much more toxic than the lead sulphate that lead workers as well as the state should aim at the elimination of the use of the carbonate in all industries in which this is possible.

2. In addition to taking other important prophylactic measures the lead workers should drink a glass of milk

between meals (say, 10 a. m. and 4 p. m.), in order to diminish the chances for any swallowed lead to be dissolved by the free hydrochloric acid of the gastric juice, as in some persons there is considerable secretion of gastric juice in the empty stomach.¹⁰

ABSTRACT OF DISCUSSION

DR. E. D. BROWN, Minneapolis: The old text-books give as the standard antidote for arsenic poisoning, which is probably the same for lead, the taking of milk, which helps to fix the acid in the gastric juice. This is undoubtedly in part the way of action. Recent investigators have shown, however, that the milk only delays the action of the arsenic and that eventually the arsenic will be absorbed and will exert its toxic effects.

MR. M. I. WILBERT, Washington, D. C.: I should like to ask Dr. Carlson whether or not he has come across the empirical practice of administering olive-oil? I know that in one large manufacturing concern in Philadelphia it has been the practice to compel the employees to take olive-oil rather liberally. They furnish all the olive-oil that the employee will take, and it is asserted that since the establishment of the practice, there has been no lead-poisoning in that particular lead-works.

DR. A. J. CARLSON, Chicago: I have no experience in giving olive-oil. Olive-oil or any fat inhibits the secretion of gastric juice; but the importance of olive-oil is probably in keeping the bowel open and overcoming constipation, which is one of the first troubles in lead-poisoning.

PHENOLSULPHONEPHTHALEIN IN ESTIMATING THE FUNCTIONAL ACTIVITY OF THE KIDNEYS

A FURTHER CONTRIBUTION TO ITS VALUE

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In a former paper Dr. Kristeller and I referred to a number of methods that have been devised for the purpose of estimating the sufficiency of the kidney function and have shown wherein they are unsatisfactory and impracticable. Up to that time we had made observations on fifty-eight subjects, giving seventy injections of phenolsulphonephthalein. These observations were made on healthy males and on a series of cases of chronic parenchymatous nephritis, acute diffuse nephritis, chronic interstitial nephritis and a few cases of enlarged prostate. The results obtained warranted the conclusion that the elimination of the drug went hand in hand with the elimination of the normal products of metabolism, a fact for which this method is bound to prove of greater value than any other devised.

We pointed out that phenolsulphonephthalein possesses the following advantages:

1. The drug does not readily decompose in solution and can be sterilized by boiling.

2. The dose required is small, 1 c.c. of the solution containing 0.006 gm. of the dye.

3. The injection is painless and is not followed by irritation if the solution is sufficiently alkaline.

4. The drug is excreted entirely by the kidneys.

5. The drug can be demonstrated in the urine in from three to ten minutes after the subcutaneous injection.

10. Hornborg: *Skandin. Arch. f. Physiol.*, 1894, xv, 209. Carlson, A. J.: *Am. Jour. Physiol.*, 1912, xxxi, 151.