LEAD INDUSTRIES ASSOCIATION

60 EAST 42ND STREET

NEW YORK 17, N. Y.

October 7, 1959

LEAD HYGIENE and
~~SAFETY BULLETIN~~
No. 134

To the Members of the Lead Industries Associations

Terminating a series of publication delays quite beyond our control, a complimentary copy of the

PROCEEDINGS OF THE LEAD HYGIENE CONFERENCE

held in Chicago last November now goes herewith to each individual in our membership who has asked to receive these bulletins. Additional copies to our members will be two dollars each, a figure well below their cost.

Our conference was without question the most important and authoritative on problems of lead hygiene in many years, and it is hoped that the papers delivered by this outstanding group of speakers will have the attention they deserve.

Manfred Bowditch
Director of Health and Safety

PROCEEDINGS

of

LEAD HYGIENE CONFERENCE

Held at

THE DRAKE HOTEL

CHICAGO, ILL.

NOVEMBER 6-7, 1958

Price $3.00

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60 EAST 42ND STREET
NEW YORK 17, N. Y.

FOREWORD

The purpose of the Lead Hygiene Conference recorded in this little volume was to make available to medical men, hygienists and interested laymen, in free and open discussion, the facts concerning plumbism which underlie present-day concepts of its causation, control and cure.

That this object was achieved seems amply evidenced by the caliber of the authorities on various aspects of lead poisoning who contributed the fruits of their experience to the program, by the quality of their presentations, by the active participation of no less than forty individuals in the discussions, and by the fact that more than one-quarter of the 140 physicians, industrialists and others present took the trouble, in letters written soon after the conference, to express their appreciation of having been included in what one old-timer termed "one of the finest groups of industrial hygiene and medical personnel that I have seen assembled in a long time."

In turn, the Lead Industries Association welcomes this opportunity again to thank all those who by their participation assured the success of the conference. For the initial printed record we are indebted to the editors and publisher of the journal Industrial Medicine and Surgery. The major revision presented within these covers attests the editorial skill of Miss Elizabeth Olmsted.

CONTENTS

LEAD HYGIENE CONFERENCE

THURSDAY, NOVEMBER 6, 1958

MORNING SESSION

Chairman

Manfred Bowditch, *Director of Health and Safety, Lead Industries Association*

AFTERNOON SESSION

Chairman

Lemuel C. McGee, M.D., *Medical Director, Hercules Powder Company, Wilmington, Delaware*

THURSDAY AFTERNOON SESSION (Cont'd)

FRIDAY, NOVEMBER 7, 1958

MORNING SESSION

Chairman
George M. Wheatley, M.D., *Third Vice President, Metropolitan Life Insurance Company, New York, N.Y.*

LUNCHEON SESSION

Chairman
Manfred Bowditch

AFTERNOON SESSION

Chairman
Manfred Bowditch

LEAD INDUSTRIES ASSOCIATION

LEAD HYGIENE CONFERENCE

November 6-7, 1958

THURSDAY MORNING SESSION

November 6, 1958

INTRODUCTION

By ROBERT L. ZIEGFELD

Secretary-Treasurer, Lead Industries Association

Ladies and Gentlemen: It is a pleasure to have the opportunity of sponsoring a meeting that includes such a distinguished gathering of guests and from which so much good may be expected. The caliber of those who have agreed to take official part in the program, and of those who have come to listen and discuss with them, most certainly indicates a fruitful conference.

For those of you who may not know too much about the Lead Industries Association, I would like to explain that it is a non-profit organization of some 70 lead-mining, smelting and refining, and manufacturing companies. While we have many functions, including sales promotion, research, technical service, economic service and the like, L.I.A. long ago recognized its responsibility in the field of lead hygiene. In the 30 years of our existence, we have sponsored considerable research in this field, and we are now gathered at our third conference of this type. More than a decade ago, this phase of our work was put under Manfred Bowditch's full-time direction.

Now, to get the important part of this meeting under way without further ado, I want to introduce your official welcomer, Mr. Felix Edgar Wormser, vice president of L.I.A. and of the St. Joseph Lead Company. Lead hygiene has long been a subject to which he has given much interested attention. He was the first secretary of L.I.A. and held the position for nearly 19 years, when he left to join his present company. Subsequently, he was president of L.I.A. for three years. He has also made great contributions through public service, having earlier this year completed five years as assistant secretary for mineral resources of the U. S. Department of the Interior. Mr. Wormser.

WELCOME

By FELIX EDGAR WORMSER

Vice President, Lead Industries Association
Vice President, St. Joseph Lead Company, New York, N. Y.

I am honored to represent the president of the Lead Industries Association, Mr. John D. Bradley, who, unfortunately, cannot be with us today. I am sure he would wish to extend you a most cordial welcome to Chicago, and to express the hope that your deliberations will result in a mutual exchange of views, beneficial not only to our industry but to mankind.

It doesn't seem possible that twenty years have elapsed since the first conference of physicians and surgeons of member companies of the Lead Industries Association was held here in Chicago at the Palmer House. It seems like yesterday to me. Some of you in this room today attended that session, and you will remember how interesting it was to listen to Dr. Joseph Aub and Dr. Fairhall, who had done so much pioneer work in the field of lead poisoning.

Years ago, I felt that the Lead Industries Association could justify its existence solely on the ground of the opportunity it had to work in the field of lead hygiene, so that the metal could be used properly and intelligently, and so that, wherever it created a hazard industrially or publicly, the proper controls could be introduced. I haven't changed my views. I think you should know that as the work of the Association has become known it has received international recognition and representation. It also has the benefit of Manfred Bowditch's great experience and knowledge in this important area. I think we can all agree that the Lead Industries Association, and the people behind it, deserve commendation for the public-spirited and frank approach they have given to the lead problem. When all is said and done, what the industries want is the truth. They can then govern themselves accordingly. Thanks to much brilliant work in medicine, participated in by many of you in my audience, the truth, pleasant or unpleasant, is certainly what they have gotten. I am sure they will also get it from this meeting.

It has always seemed to me that there is no reason why a wonderful metal such as lead, bestowed upon us by a bountiful nature, can't be used safely and beneficially by all of us. It would be difficult to conceive of an economy where this indispensable metal no longer was available to us. It has so many everyday uses that we take for granted, especially in driving our automobiles.

Although my incumbency in Washington kept me away from observing the steady progress that the medical profession was making in studying the lead hazards and related problems, I am sure we all recognize that many medical research developments since our first conference have given us an assurance that we previously did not possess. No doubt there is still a lot of educational work that has to be done where ignorance about lead's properties or uses still prevails.

But I did not come here to take the time of this important meeting any longer than to express my own personal delight at being here as an interested listener. I am sure that out of this conference much good will come, and I wish you every success.

I now take pleasure in turning this meeting over to our chairman, Mr. Bowditch.

CHAIRMAN MANFRED BOWDITCH: The first of our technical papers will be by Dr. Elston L. Belknap, who has been connected with the storage battery industry longer than I can remember.

DR. BELKNAP: It is a pleasure to be with you again. It seems just yesterday that we had the conference symposium here that took place ten years ago. I would also like to say that although it doesn't appear on the program, the co-author of this paper is my son, who is here with me today. He was associated with me for a considerable time in some of this work and is now doing research in hematology, and teaching at the University of Wisconsin.

CLINICAL CONTROL OF HEALTH IN THE STORAGE BATTERY INDUSTRY

By ELSTON L. BELKNAP, M.D.

When the senior author was first engaged as a consultant medical director of a large battery company in 1930, the general manager asked that management be advised once a month regarding the level of lead absorption in the workers. He also said, "Make your recommendations ideal -- aim at the stars for what you think should be done to prevent lead absorption but don't be surprised if we don't put into effect all the recommendations at once. However, keep after us and gradually we will put them into effect as soon as we can work them into our production schedules." Over the years, the company and their insurance carrier have been slowly but faithfully improving protective engineering ventilation designed to collect lead dust at its source. The company is Globe Union, Inc., and the insurance carrier, Employers Mutual of Wausau.

Both by frequent plant tours and their correlation with physical and laboratory examinations of the men, the Medical Department has been able to point out definite points at work places where production equipment was defective or inadequate regarding dust collection, thus causing increased lead absorption. However, with the increasing speed of modern machines, the potential lead hazard has been multiplied rapidly. In most instances we have all felt that we were working as a team — foreman, superintendent, engineers, general manager and the lead-exposed workmen themselves, as well as the Medical Department — in a determined effort to reduce human lead absorption as rapidly as practical.

The result of this teamwork is demonstrated by the reduction of the rate of disabling lead intoxication from 20% in 1929 to 2% or 3% within the first six years, and by the fact that thereafter disabling lead intoxication or true lead poisoning has averaged only one every other year, and none at all the last two years. All of these cases were of the simple lead colic type and were never complicated with lead palsy or encephalopathy. (Figure 1)

The year 1929 was known to some of you as the great financial crash. That was the year just before I came to the company when there was the greatest incidence of disabling lead intoxication. Then it tapered off fairly rapidly when we sorted out our most heavily exposed workers and had a very cooperative engineering group working to reduce the lead exposure. There was a long period, from 1935 to 1950, when we had only one case of lead intoxication.

Again in 1955, there was a peak of five cases. This was the time when automobile production the country over was at its peak, and we were working in many instances 10 hours a day, six days a week, all contributing to increased lead exposure and absorption.

When you have less time to get rid of lead, if there is any break in technique in protection, you will immediately see the response in increased lead absorption. For the last 22 years, the Medical Department has always been able to warn management and the men themselves of heavy lead absorption, so that the men could be moved pending a reduction of lead exposure. In the eight years from 1935 to 1944, and the five years from 1944 to 1950, there were no cases at all. (Figure 1) In all cases of actual disabling lead poisoning there has been engineering breakdown or delayed repair of faulty engineering ventilation equipment, or even carelessness of some of the men in using the respirators.

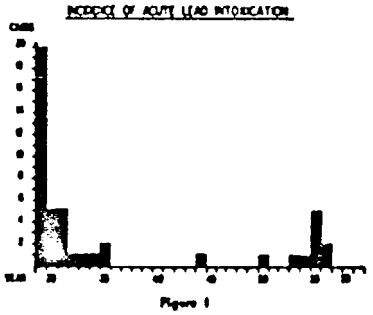

Figure 1

Concurrently with the Medical Department's warnings gained from qualitative tests, the engineering protection has been in a process of steady improvement. This has included the installation of a very effective dust disposal system with a bag house used on the machines which give off the greatest amount of lead dust in addition to the cyclone system collecting lead dust at other points of its evolution. During the process of improving the engineering control, so as not to interfere with the necessary production, certain men have been equipped with respirators, both the regular face masks (Bureau of Mines Approved) as well as positive pressure airline masks in certain cases. Current samples show that all are now under the safe limit of

2 mg per 10 cubic meters except two instances of 3.3 mg and one of 2.35 mg contrasting the high levels from 1944 to 1954 where air samples in seven instances varied from 7 mg to 23 mg. (Figure 3)

Over the past 28 years, the working environment has progressed from uncontrolled lead exposure in the totally unprotected work of hand mixing and hand pasting, on through the use of the early automatic machines which were not well exhausted, and finally up to the modern mixing, pasting and assembly, high-production machines where a great amount of engineering ventilation equipment has been built into the machines from the moment of their first design.

For 28 years we have had the opportunity to study clinically a slowly changing group of 50 to 100 men who have been exposed to the inhalation of lead in varying concentrations in storage battery manufacture. While there has been some

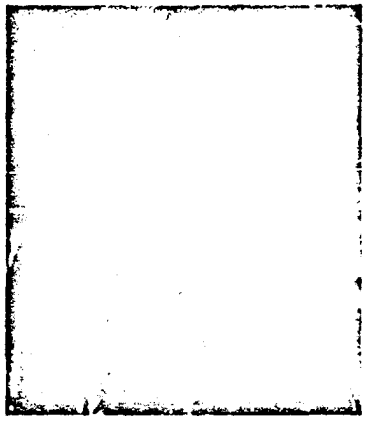

Figure 2

change of personnel, our labor turnover has been very small, so that the majority of our men have been working in this same plant from five to 30 years. From the beginning, our work in the diagnosis of lead absorption has been based on the pioneering work of Aub, Fairhall, Minot, Reznikoff, and Alice Hamilton.[1]

In this series of cases we have depended chiefly upon the careful clinical examination of each worker at frequent intervals of from two to four weeks, depending upon the concentration of his lead exposure. The physicians have been trained in the general field of diagnostic medicine. This has included using the medical skills of history, physical examination including a search for lead line of the gums under a lens (Figure 2), observation of the blood pressure and the strength of the extensor muscles, as well as laboratory studies including hemoglobin, number of stippled red cells per 50 high power oil immersion fields, a routine urine, and qualitative tests of urine for coproporphyrin.

In various learned circles, I have been somewhat shocked when physicians have said that there may not be any such thing as a lead line simply because they have never seen it. If you will look at the upper left incisor area in Figure 2, the left central incisor, opposite the base of the tooth, you will see the "lead" line. In the gum, not on the teeth, there is a row of dots or striate marks which means a deposit probably of lead sulphide in the gums. This will not wash off, and it will only disappear when there is a reduced amount of concentration of lead within the organism.

I know in the past that Dr. Aub used to have his residents take a small section of this gum line and look at it under the microscope, then one can see a black deposit directly under the mucosa. So here is the famous "lead line" that was described over 100 years ago before the Royal Society, and known since as the Burtonian line. Incidentally, all of those cases were cases where lead salts had been used as internal medication, nonoccupationally, in the treatment of patients in the hospital at that time.

We have changed our therapy somewhat and do not prescribe lead internally any more, but the lead line from occupational exposure exists as described originally by Dr. Burton. I spent a little time on that because there has been some argument as to whether there is such a thing as a lead line.

In addition to the clinical examination of the patient and the base-line laboratory studies listed above, there has been clinical evaluation of the work place in regard to lead dust inhalation in the storage battery plant by the same physician. This involves study and correlation of the worker's actual operations on his job, together with the physician's knowledge of his general physical condition and personal habits, along with a medical evaluation of the level of his lead absorption. Whenever a man showed danger signals indicating the probability of an impending disabling lead intoxication, he was either moved or given a positive pressure airline respirator while engineering protection was being installed or improved. In 1956, in two cases of threatened acute lead intoxication, expected time off from work owing to lead poisoning therapy was reduced from a period of several weeks to a few days by a course of intravenous Calcium EDTA under a hospital regime as de-

LEAD ABSORPTION

Case	Clinical and Qualitative Tests - 1958						Quantitative Tests - 1958				
	Pb Line Gums	Stipple Cells 50 Fds	Hemoglobin Gms.	Hct %	Porphyrins Plus	Porphyria Micrograms 24 hr	Pb Urine Mg/L*	Pb Blood Mg/100cc	Pb Air Mg/10cu m	Pb Air Av. 1944-1954 Inst.
1	False	7	12.3	79	43	4	2700	0.39	0.118	2.35	7.50
2	1+	14	13.6	86	42	4	480	0.37	0.116	1.4	23.86
3	False	15	10.3	66	36	2	645	0.36	0.095	0.35	7.81
4	2+	10	13.8	86	42	3	1305	0.31	0.100	0.35	1.22
5	False	7	9.8	62	34	2	2085	0.31	0.175	0.35	0.56
6	0	12	11.6	73	41	3	180	0.30	0.081	0.6	0.54
7	0	17	11.3	73	39	4	875	0.26	0.097	1.27	3.62
8	0	4	12.6	80	44	4	1066	0.26	0.094	3.30	21.87
9	0	10	12.4	79	43	3	945	0.26	0.118	3.30	21.87
10	False	14	12.4	79	40	3	240	0.26	0.099	0.22	2.46
11	0	7	12.7	82	42	4	2180	0.24	0.099	0.97	3.31
12	0	6	12.7	82	46	4	1290	0.19	0.138	0.35	2.93
13	0	20	12.7	82	41	3	885	0.17	0.095	1.41	3.84
14	2+	23	11.8	76	39	4	2375	0.16	0.062	0.35	2.93
15	0	0	12.7	87	44	3	1020	0.12	0.102	0.94	7.89

*Adjusted to mean specific gravity (1.024)

Figure 3

scribed elsewhere.[9] No oral Calcium EDTA has ever been given to workers in this plant.

Years ago, collection of 24-hour urines for quantitative lead determination was done every few months to supplement the repeated clinical examination and the simple qualitative tests which were performed every two weeks. This was carried out for 15 years, from 1932 to 1947. However, it was found that the information gained by this more refined test of quantitative lead in the urine was of no more practical value than the simpler tests. In fact, it did not answer as helpful in our personal study of the individual worker as did the original tests of lead line of gums, strength of wrists, hemoglobin, stippled cell count and, later, urine for porphyria. Though the Medical Department had often been urged to substitute quantitative studies of the urine for lead as a screening test in place of the lead line and stippled cell study, we became convinced that quantitative lead in the urine study *alone* was not safe. Therefore, study of the lead line, hemoglobin and stippled cell counts was continued throughout the entire 28 years of chiefly medical control of lead absorption in the worker. Routine examination of urine for qualitative test for coproporphyrinuria has also been done for the past nine years as a helpful adjunct leading to a diagnosis of lead absorption. We still believe it has basic implications in the metabolism of lead.[2,4,5,6] A number of authors and clinical workers in the field have noted that qualitative porphyria tests are of distinct value in suggesting lead absorption becoming positive before stippled cells appear.[7,8,9,10]

Recently this whole question of lead absorption and intoxication has been here reevaluated as measured by both qualitative and quantitative laboratory determinations. This intensive study involved 15 men, two of whom had worked for three years, five for six years, two for 11 to 12 years and six from 20 to 32 years. They had all been exposed to heavy lead inhalation from time to time. It was already known that they had definite evidence of lead absorption because of the simple though frequent serial studies of history, physical examination, and qualitative blood and urine studies. Three men now have faint but definite lead lines and the majority have had on occasion stippled cell counts of from 10 to 25 per 50 oil immersion fields. These 15 men were chosen before there was any knowledge of their exact blood or urine quantitative values for lead. The clinical and qualitative tests alone had already shown that lead absorption was quite high and that these particular men needed to be watched closely. (Figure 3)

You will see on the left the columns for qualitative tests, and on the right those for quantitative tests.

In regard to lead exposure, as seen by air analyses, the last column of figures on the right represents the average exposure covering a period of air analyses from 1941 to 1954. I am sure that you will see there have been some fairly high levels. This is the amount of lead in the air per 10 cubic meters, and if you wish to reduce its values per one cubic meter, just move the decimal point to the left.

The column next to the right is the most recent air analysis, and you see it has dropped sharply. This was done in 1958. However, in three instances, we are still slightly over the permitted level of 2.0 mg per 10 cubic meters, namely, 2.3 mg and 2.35 mg.

These cases, as I have said before, are arranged according to decreasing concentration of lead in the urine. That is perhaps the most important correlation. I would like to point out that, in these 15 cases where we were trying to see if the quantitative lead gave us any information which the qualitative tests did not give, such information is noted in only one case, number eight. This was a man who was once heavily exposed to this concentration of well over 21 mg, though now only 2.3 mg per 10 cubic meters of air. He was using an airline respirator most of the time. There were certain periods when he had to take it off for machine repairs. He never showed a lead line. He, incidentally, is the man that has worked 22 years and is now "in the pink" physically.

He had only four stippled cells, hemoglobin was 80%, or 12.6 gm, and he nearly always has had a 4 plus porphyrin test in the urine.

You see, in all instances except one, that these cases show a three to four plus porphyrin.

In this case, number eight, the lead line level in the urine is .26 and in the blood .086. This is over the so-called safe level of lead in the urine of .15; but the blood is not much over the so-called upper limits of the normal of .07. Many have said that if we have a reading of lead in the urine of over .2, that is a level compatible with a consistent state of lead intoxication. However, such a urine lead level certainly of itself is not diagnostic of lead poisoning. Some of these urine values run quite high; even as high as .39. Also, the blood leads in many instances run high, but the men show no symptoms.

Now I would like to point out case 14 to balance case eight. In case eight, we had very little evidence by qualitative tests of heavy lead absorption. In case 14, there was the safe limit of lead in the urine, .14, and in the blood .06, but on qualitative tests he had a two plus lead line, 22 stippled cells, with 76% hemoglobin, and a four plus porphyrin. Here the qualitative tests score over the quantitative tests.

In Figure 2, his highest lead exposure was 2.9, but more recently only 0.55. He is working in charge of automatic casting where ordinarily we think there is very little exposure. We know that when the lead oxide contaminated scrap parts come over from the pasting line, they are dumped on a belt and go back into the pot.

We have had suction at the point of dumping, but are now placing suction around the conveyer belt itself.

There was no clinical evidence that serious, irreversible damage had been done to these men by this degree of lead absorption. If it had been felt that transient periods of increased lead absorption were likely to cause serious organic damage with residuals, we would not have relied entirely on the more easily available tests which are a measure of the individual's body reaction to lead. We wished especially to determine whether evidence of impending lead intoxication could be more sharply predicted by quantitative tests of urine and blood lead, rather than by the more easily obtainable tests that we had been using for many years.

What does this recent work on a small group of lead absorption cases from the storage battery industry show as regards the use of qualitative tests contrasting the use of complicated quantitative tests used in a search for early cases of significant lead absorption? By significant is meant cases where disabling lead intoxication is likely to occur in one to three months if no immediate effort is made to reduce the lead exposure. This can be done either by moving the worker or by insistence on the use of appropriate respirators while defects in mechanical protective equipment are being corrected.

In 13 of 15 men there was evidence of heavy lead absorption by both types of tests. In only one case (number eight in Figure 3) the simple qualitative tests erred in showing only minimal evidence of lead absorption by stippled cell and porphyria, though the quantitative tests showed definite though moderate indications of fairly heavy lead absorption. This is the case where the air concentration has frequently been over the safe limits of 2 mg per 10 cubic meters of air. The operator is a rather conscientious user of the positive pressure respirator supplied him. Not long ago his lead exposure shown by air samples was as high as 21 mg per 10 cubic meters, about seven times the recent reading of 2.2. This man had worked first as a hand mixer and then as a pasting machine operator for 22 years. At no time has he ever had even minimal symptoms suggestive of a possible lead intoxication, but we have watched him closely and recommended improvements in his engineering protection.

The quantitative tests erred in one case (number 14, Figure 3) by showing normal limits of lead in urine and blood, while the qualitative tests warned of dangerous lead absorption shown by lead line, stippled cell and coproporphyrin in the urine as well as a moderate secondary anemia. This individual has never been ill, though he has worked in this storage battery plant 24 years. Much improved engineering protection has been given him and more is planned.

Aside from these two cases, the remaining 12 showed that the individuals had potentially dangerous levels of lead absorption as measured by both qualitative and quantitative studies of lead in urine and blood.

The advantages and disadvantages of the two types of tests may be analyzed as follows:

I. The advantages of the clinical and qualitative tests.

A. Practicability, with the necessity of drawing only a few drops of blood and with only a very small amount of time demanded of the men away from their work.

B. Speed of determination is noteworthy, taking only 15 minutes in case of each stippled cell count.

C. There is no likelihood of lead contamination.

D. This method measures both lead absorption and intoxication in individual cases.

II. The chief disadvantage of the clinical and qualitative tests is that theoretically they are not "specific" for lead.

A. The lead line is indistinguishable from a bismuth line which formerly was quite common when bismuth was used for the treatment of syphilis. At the present time penicillin therapy has replaced the use of bismuth. The theoretical possibilities of a lead line being confused with mercury, thallium or silver are very unlikely because of the character and rarity of such findings, particularly in a known lead worker.

B. Stippled cells are not specific because they may be found with any severe anemia with a low hemoglobin due to carcinoma, Hodgkin's disease or leukemia. In lead intoxication, however, stippled cells are usually plentiful with a normal or very slight reduction in hemoglobin. As Cabot pointed out in 1911, the finding of many stippled cells with a relatively slight drop in hemoglobin is characteristic of lead intoxication. It is not our belief that any one spot count of stippled cells is diagnostic. With three or four stippled cells we hire men as within normal limits. When studying a lead worker, if his stippled cell count rises quite rapidly within a few days from a base-line of six to 10 up to 15 or 20 or over, one can predict that there has been a breakdown of engineering protection such as with a blocked exhaust pipe or cracked lead pot. If the stippled cell curve continues to rise sharply when checked every two or five days, the man can be moved before lead intoxication occurs.

C. Coproporphyrins in the urine may be markedly positive due to other intoxicants such as alcohol and barbiturates, but in the known lead worker its finding in a frank four plus cerise color is most likely to indicate coproporphyrinuria from lead absorption.

III. The advantages of the quantitative tests are:

A. They can be done entirely by nonmedical and nontechnical personnel.

B. They can give a relatively rapid screening report on the level of lead absorption in a large number of workers — 100 or over.

C. These tests are truly specific only for lead.

IV. Disadvantages of relying entirely on the quantitative tests are:

A. There is the possibility of contamination in collection of urine and blood samples, as well as the objection of the men themselves to obtaining adequate overnight urines or a large 10 cc blood sample from the vein instead of a few drops from the ear. Even the advocates of the quantitative study of blood and the urine warn of the danger of lead contamination of such samples.[31,32]

B. There is paucity of clinical laboratories equipped to give accurate reports from quantitative studies of very minute quantities of lead found in blood or urine.

C. These tests measure lead absorption only and do not make a diagnosis of lead intoxication. They do not show the effect of lead on a given individual.

Comment

Determination of stippled cells in cases of lead absorption and lead intoxication is still of great significance. Besides our own experience, this is borne out by published papers of other men with experience in this field.[33,34] In whatever manner lead absorption is diagnosed and apart from the usually transient three types of lead intoxication listed below, the question arises as to whether lead absorption per se has done any irreversible damage to the organism. Aside from lead colic, with or without anemia, which occurs in 90% of the cases as the commonest type of lead intoxication from which the patient usually recovers without residual, there are the rare 5% or 6% of cases with lead palsies. Though these may occasionally show residual, such complications are rare if properly treated

LEAD ABSORPTION — 15 cases — Clinical Findings

Case	Occupation	Years Worked	Symptoms	Blood Pressure On hire	Blood Pressure Present	Urine, Albumin & Microscopic	Total Serum Protein*	Recommendation
1	A. Group	11	0	142/100	120/90	Negative	7.22	Give Pos. Rec.
2	P. Salvage	6	0	140/90	130/90	Negative	7.23	Watch Rec.
3	P. Impos.	6	1956 Colic	140/90	122/82	Negative	6.86	Move & Iron
4	A. Dry chg.	12	0	130/90	130/90	Negative	7.23	Ventilation
5	P. Impos	6	0	120/80	130/90	Negative	7.23	Move & Iron
6	Cast Impos.	3	0	140/90	130/90	Negative	6.84	Give Resp.
7	C. Wable	25	0	112/70	120/80	Negative	6.68	Watch Rec.
8	P. Oper.	22	0	120/70	130/90	Negative	6.68	Watch Rec.
9	P. Oper.	22	0	130/70	110/80	Negative	7.42	Watch Rec.
10	C. Pe	20	0	140/90	170/100	Negative	6.34	Watch Rec.
11	M. Cycle	20	0	100/70	102/60	Negative	7.84	Watch
12	C. Auto	6	1956 Colic	110/70	120/80	Negative	6.88	Ventilation
13	A. Stock	3	0	122/72	112/80	Negative	6.86	Watch Rec.
14	C. Auto	24	0	120/70	130/80	Negative	7.84	Ventilation
15	A. Reeler	6	0	114/72	124/82	Negative	6.86	O.K.

*Normal range 6-8 gms.

Figure 4

over an expected healing period of three months to three years. In the very rare instances of lead encephalopathy occurring in adult workers in modern industry, if the patient recovers there are usually no sequelae.[15]

The search for hidden residuals of lead absorption should go forward. For example, there may be a transient, nondisabling secondary anemia as shown here in two cases of the 15 cases presented in this study (numbers three and five, Figure 3). They are being given iron and will be moved temporarily from further heavy lead exposure. We are also constantly searching for possible objective evidence of any permanent injury from chronic lead absorption.

Figure 4 shows the years worked and the symptoms and blood pressure for comparison with the time when the men were hired many years ago, and now within the last month. In only one case was there a rise in blood pressure and that not too much.

This correlates with the report that we made previously on blood pressure in workers in the lead industry studied over a five-year time, and also with the report and comments by Dr. Mayers and Dr. Hamilton as to the fact that there does not seem to be any definite correlation between long, continued lead absorption and an increase in blood pressure.

The routine urines studied for microscopic findings and albumin were all negative, and in addition, the total serum proteins were all within normal range.

In our own experience and knowledge of the literature, we are led to believe that mere lead absorption without the symptoms of lead palsy or encephalopathy causes no permanent physical harm to the adult human. Further, apart from those rare cases of colic with short periods of acute disability, there is no increase in plant absenteeism or loss of work ability in our experience. There is also no weight loss, no consistent blood pressure abnormality and no damage to the kidney as measured by routine urine analysis, while one sees no evidence of liver damage either in the form of jaundice or in the estimation of total protein. (Figure 4)

We would welcome reports of cases of other workers in the field where the qualitative tests mentioned above are followed out routinely and in detail by a physician together with the more complex quantitative tests of lead absorption.

Conclusions

1. Together with clinical examination and evaluation by a physician, the qualitative tests of stippled cell, hemoglobin and urine porphyrin have proved effective in estimating levels of lead absorption. This is true in the majority of lead-exposed workers observed in this storage battery

to warn of heavy lead absorption in time for moving or otherwise protecting the men, except in the rare instance where management or worker have been unable to cooperate immediately in the recommendations of the medical department.

3. Quantitative examination of the urine for lead is a useful supplementary aid in evaluating lead absorption in those instances where large industry is financially able to support this complicated and somewhat difficult test.

4. Blood lead tests, though requiring great care both in avoidance of contamination and in complicated chemical manipulation, are of great value for medicolegal and research problems. They have not seemed practical for the routine study of the individual with lead absorption in the average lead storage battery plant.

5. Qualitative and quantitative blood or urine tests for lead are not of themselves diagnostic of lead intoxication. They are merely signs of lead absorption to be judged by the physician in the light of the whole clinical picture.

6. Frequent clinical examinations of worker and workplace by the same medical observer, together with qualitative studies of blood for hemoglobin and stippled cells examined serially every few days, as well as occasional urine porphyrin tests, are of most practical help to a physician experienced in the clinical control of health in the storage battery industry.

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CHAIRMAN BOWDITCH: As you will have noted from the program, a discussion leader has been appointed to lead the discussion following each of the papers. Mr. William Pallies will lead the discussion of Dr. Belknap's paper.

DISCUSSION

MR. WILLIAM M. PALLIES: I think one of the big problems we have here is defining lead intoxication, and as far as I can see from a workmen's compensation point of view, things are gradually changing and the social climate has brought more and more things under the workmen's compensation laws.

I think we will have more and more of these little illnesses which have occurred and have been passed off before, which will now be called lead intoxication. So my contention is that we must set limits on urine and blood leads, and then say that as far as we can see, if anybody exceeds these, there may be trouble; the man is going to develop lead intoxication or he is going to have a good legal claim. If we have the evidence of urine and blood leads which exceed what we consider dangerous levels, then the Industrial Commission is going to consider that the man has lead intoxication.

To me, *Figure 3* demonstrates very clearly something which I have held all along. When you examine the blood lead levels, with few exceptions they are all in excess of .08 mg per 100 gm of blood, which we have always considered to be a dangerous level, and these men should all be removed from exposure to lead except possibly number 14.

I don't understand number 14. He has a lead line. He has four plus porphyrin, but he certainly isn't showing any great lead exposure as far as blood urine lead levels are concerned. Other than that case, the urines, the bloods, the porphyrins and possibly the low hemoglobins indicate that these men have been exposed or are being exposed to too much lead. So I would substantiate a case from this figure for the quantitative studies.

MR. PAUL REZNIKOFF: It would be a grave mistake if we made any diagnosis of lead poisoning on the basis of the amount of lead in the urine or blood. If we try to make our diagnosis on the basis of what we think compensation boards or industrial medical boards might say, we would not be making our diagnosis on a medical basis.

I agree with Dr. Belknap and the industrial hygienists who say that the actual quantity of lead in the atmosphere, of lead in the blood, of lead in the urine are all guides, but the diagnosis of lead poisoning should be based on disability due to lead, and not on chemical findings.

doesn't make the diagnosis in the individual case.

MR. PALLISER: Being an industrial hygienist, I am not interested in diagnosing lead intoxication. What I am trying to do is minimize the exposure, and I have depended on the medical authorities to set certain limits which have worked out pretty well for us in the electric storage company.

When we have kept lead levels below about .2 in urine and .08 in blood, we have had no trouble whatsoever. So we really have had no lead intoxication to diagnose.

DR. E. A. REINCE: I do not intend to enter into a discussion, or to express a difference of opinion with reference to the diagnosis of lead poisoning. I think it may be said, once and for all, that the diagnosis of lead poisoning is made only where actual illness exists, and then only by clinical means. If the individual is ill in any way that can be demonstrated on the faintest evidence or the greatest, we may then make a diagnosis of lead poisoning. I call attention to the fact that every man in the group represented by Dr. Belknap's figure had a four plus porphyrin. I don't know precisely what that means, because its significance is related to the nature and the precision of the test that was carried out. Moreover, this test is nonspecific, with respect to its relation to lead as the cause of the abnormality, as are all the other so-called nonquantitative findings. Nevertheless, the appearance of abnormal quantities of porphyrins in the urine, if they can be attributed to lead and lead absorption, are, I believe, the first sign of the existence of lead intoxication.

Whether it is followed by severe disabling illness is another matter, and we do, I think, have to recognize that there are men who do not develop palsy or encephalopathy or colic, but do develop hematol ;ic signs of lead intoxication.

There are many other things that could be said, but I think it should be said that this abnormal finding indicates quite clearly that the industrial hygiene in the lead storage battery manufacturing industry, if this were a representative illustration of it, is not yet good enough. What we are talking about when we apply standards of analytical precision to the blood and urine is not the diagnosis of lead poisoning, but the recognition of the existence of danger, and there are adequate experimental and observational data that demonstrate quite clearly the relationship, the correlation, between the analytical findings (if you can determine the level of lead excretion by the analysis of a sufficient number of samples, or if you can measure the general level of the lead absorption in the body by means of analyses of the blood), and the degree of danger associated with the occupational exposure.

Thus, we may say that an individual is not in danger if the analytical values are below a certain point; we may also say that the danger increases, the danger of the occurrence of intoxication and the degree of its severity will increase as these values range upward above certain critical levels. This is, therefore, not a question of diagnosis. It is in the lead trades as cranks men to work without danger, we have done a good job. Until we have done that, we have not done enough.

DR. J. H. PATTERN: I agree with the discussion leader. The function of the physician in industry is to prevent. Diagnosis is an indication that we have failed. Prevention is a far more difficult thing than diagnosis, and in prevention we are virtually trying to discover whether a crime is being committed, not has been committed; and all the evidence we can get, qualitative or quantitative, which, when added together, shows that a crime is being committed, is what we need.

In view of what Dr. Rendtorff said about the porphyrins, there is another very interesting observation in another field of medical science. Recently Borsook of Cal Tech, in studying the incorporation of amino acids into proteins, found that the incorporation of amino acids into reticulocytes is greatly hindered by many compounds of which the most active is lead, that a molecular concentration which corresponds to the level in the blood of lead, which we look upon as a sort of borderline between a serious lead hazard and one that we can ignore, is a level at which lead in Borsook's experiments prevented incorporation of amino acids into reticulocytes, and therefore, the metabolism of hemoglobin.

MR. PALLISER: I was very happy to see these results, especially on porphyrins. I have been asked many times about what to do, in a small plant where 20 or 30 people are exposed to lead. A complete laboratory set up to do urine and blood leads is out of the question. Yet, something must be done. In such a situation I recommend urine porphyrin analysis.

I think Dr. Belknap's work on these 18 men demonstrates the value of porphyrin analysis, and apparently he is backed up by some of the people here today.

DR. BELKNAP: I would simply say in closing this discussion, that I have made no claims to indicate that ours is a perfect situation as yet, but I think you will see I have pulled no punches. I have given you the facts on what high levels of lead absorption we have, and it is obvious that we should aim to reduce them.

However, in this plant, as in the majority of middle-size to small battery plants, where they have no access to reliable urine or blood lead determinations, I have given you something of a yardstick for lead absorption. I believe this will hold in keeping people clinically well while we are reducing the lead exposure.

As Dr. Rendtorff said, the diagnosis of lead poisoning finally is a medical problem, and in our part of the country the Industrial Commission boards place great weight on the decision of the physician as to whether a patient is really suffering from lead intoxication, or whether he has other coexistent illnesses.

They usually pay compensation as yet only for disabling lead intoxication. It is quite obvious the flood of claims which might develop in certain areas

I believe that such quantitative tests are valuable in helping point out danger spots, but I expect to continue to use our periodic qualitative or nonspecific tests, and at the same time attempt to reduce the level of lead exposure.

CHAIRMAN BOWDITCH: As is stated at the end of the program, if it is desired to have

after lunch. That was done at the last of these conferences, and it enabled various people to get things off their chests that there wasn't time for during the conference itself.

We now pass from the storage battery industry to the ceramic industry, and Mr. Russell W. Frank, who is the Safety Director of the Ferro Corporation with headquarters in Cleveland, is going to tell us about "Health Control in the Ceramic Industry."

HEALTH CONTROL IN THE CERAMIC INDUSTRY

By RUSSELL W. FRANK

To a considerable extent, our report is designed to demonstrate an approach to a lead control problem that has been successful and may contain suggestions for industrial health workers faced with the same problem in the future.

We manufacture several hundred glass formulae for use as protective and decorative coatings for metal and clay. We are the world's largest supplier of these products, but when compared to the total glass and ceramic industries, we represent only a small, specialized portion.

Our operations demonstrate a lead exposure problem less significant than that of other industries using lead, because lead in glass complexes presents a different degree of solubility than in other forms. We also demonstrate the importance of recognizing that solubility is increased as the particle size decreases and presents more surface area for chemical action.

Our fritted glasses, porcelain enamel for metal, and glaze for clay bodies, range from the simple lead borates to lead-sodium-aluminum-potassium-calcium-boro-silicates. The lead content varies from 2% or 3% to 70%. Our glasses have unique characteristics, among which is to resist attack from certain types of exposure. The best known is an acid-resisting glass. Our glasses mature or fire onto metal or clay at temperatures ranging from 980° F to 2500° F. The metal coatings require a relatively short exposure to maturing temperatures, sometimes a matter of a few seconds. The glass coatings for clay bodies must be designed to mature with several hours exposure at higher temperatures.

At present, only a few of our production items contain lead. One plant uses up to 80,000 pounds of litharge per week compared with the weekly production of 870,300 pounds of glass. The average is less than 10% of the number of production items containing lead.

One part of our industry effectively demonstrates a singular lack of lead phobia. The pottery industry is changing from raw glazes to fritted glazes which provide lead, where essential, in a less soluble form.

The Great Britain "Pottery Act," which is now more than ten years old, reads: "Use lead (and some other toxic materials) properly and you should experience no trouble. To help you, our agency has much experience and this should be applied to your process."

My personal introduction to the lead problem occurred with my assignment as Safety Director of Ferro Corporation about ten years ago. As any safety engineer will do when accepting a new assignment, I surveyed the problems contained within that assignment and I identified the problems that should have the priority of attention and work. My survey was not completed before an employee began showing symptoms of acute lead intoxication.

Following the then prevalent practice in industry with lead exposures, we screened all employees in our plant and laboratories with the stippled cell count technique. To assist our Medical Director, Dr. W. W. Markley, all available literature was reviewed. At that time, the literature contained almost no reference to the solubility of lead glass compounds. We did find data relating to coproporphyria presence in urine in lead exposures. The deLang and TenBerg test was immediately added to our battery of screening tests. The initial results were very encouraging. A qualified medical technician was employed to continue the work of testing each exposed employee each month with the porphyria check and the stippled cell check.

The results showed acceptable correlation. The conservative medical judgment that had to be applied indicated the desirability of more exten-

sive laboratory work. Acting on this judgment, management provided a completely equipped laboratory and authorized the employment of a biochemist.

Several meetings were held involving plant supervision, plant employees and the officers of our union. The purpose of these meetings was to acquaint the men with our goals and the methods elected to reach them. The meetings contained an admission of our inexperience and a guarantee that the entire program would be conducted in the open.

Ten years ago, this approach to a problem of this type was discouraged by some lead industries. Looking back, we have never had any reason to regret our action. Today our plant and laboratory personnel have full access to their lead report records and, as a result of the indoctrination and training, frequently help us pinpoint their lapses in working techniques that produce slight elevations in lead signs. They demonstrate no lead phobia. We have had no cases of lead intoxication.

We can report only two or three situations in 10 years wherein the family doctor of one of our employees with vague gastric disturbances found it necessary to make a tentative diagnosis of lead poisoning, the familiar difficulty of lead industries' medical departments.

Our effective control measures now include: (1) Two changes of clothing per week. (2) Regular bathing from daily to biweekly depending on job assignment. (3) No smoking and eating without prior washing of face and hands. (4) Smoking and eating prohibitions in production areas. (5) Daily issue of a clean respirator. Each employee is assigned two. Only three areas are "respirator areas," yet a number of employees voluntarily use respirators in other areas. We encourage this because our glasses contain silicon, chrome, zirconium, antimony, potassium, copper, manganese, nickle, boron, strontium and cadmium, to name a few. (6) Dual lockers: one for street clothing and one for work clothing.

Our laboratory work included comparisons of quantitative and qualitative porphyria findings in the urine with blood leads, urinary leads, and stippled red counts.

We believe the porphyria check provided a better lead-screening examination than could be obtained by examining blood smears. We estimated 15% greater accuracy. We were faced with an occasional negative blood smear which was not supported by a negative porphyria. In addition, the laboratory conclusively demonstrated the value of the following points: (1) The specimens were more cheerfully given by the employees. (2) Time and trouble to obtain and process the specimens were greatly reduced. (3) We included, and still do, a porphyria examination on the pre-employment urine specimen which is a part of our complete clinical examination.

This side light is interesting because we started the practice in an effort to provide a type of control for our work. Our medical department has continued the practice because a positive porphyria in any degree, as a part of the pre-employment physical examination, should be checked out. It is a sign something is wrong. Briefly, our checking out has revealed a few cases of uncontrolled pre-occupational exposure to lead, some rather significant respiratory conditions and two documented carcinomas.

This type of screening examination now has the approval of our State Department of Health. We use it in four plants and the new aluminum enameling industry shows a preference for the technique. In a few cases I have provided precise standards and taught lay plant employees to perform the test. We offset the question of lay evaluation of results by requiring medical supervision of all positive specimens.

Under normal circumstances, an employee will produce a negative porphyria as a part of the pre-employment examination. From two to six weeks following his start to work in the lead exposure, he will demonstrate an elevated porphyria, usually of the plus one or plus two variety. Within two to six weeks, the elevation disappears. We presume this is accounted for by the fact that his physiology is adjusted to the new environment and is operating so as to receive and discharge lead below the maximum permissible level. I will not dispute that new employee indoctrination produces a degree of adjustment in personal habits and hygiene which could produce the same results. Both points have value in teaching employees.

Each month we publish a graphic demonstration of the lead volume processed by the plant. We think this is important in our role of placing all the cards on the table. Early in our efforts to educate the employees, it was possible to trace certain lead production items, department by department through the plant, by screening test results. Today, with the engineering changes and improved employee education and attitude, it is no longer possible to do this. In fact, we now find it difficult to obtain a large enough group of employees with significant positive porphyrias from screening tests to obtain blood and urinary leads to make the necessary cross-checks we think should be a part of a conservative attitude in our control program.

In our plant we test 800 employees per month. In general, trace and plus one positives are of the greatest interest to the employees, nurses and

the Safety Department as they may indicate individual or group trends. Plus two's are referred to the medical director and immediate supervisor. The supervisor reviews working techniques. The doctor's check includes weekly "porphyrin checks." Depending on clinical findings, employees' histories of sensitivity to lead, blood and urinary leads are ordered from two plus to four plus. One year produced so few three and four pluses that we enlarged the group to include two plus positives to obtain 15 or 20 blood and urinary leads as checks per year for control. Employee job changes out of lead exposure areas are usually only necessary in the four plus range and then only if the employee has two consecutive weekly checks producing four plus.

I believe that the published maximum allowable concentration of 20 milligrams per cubic meter of air should be revised to provide a suggested allowable concentration for each lead compound. Our lead compounds range from 2% to 70% elemental lead and we have obtained air values up to 60 milligrams of lead per cubic meter with the employees showing zero elevation in lead absorption signs.

In our case, the probability of the plant working on one lead compound exclusively long enough to obtain samples is remote. We usually have several adjacent smelters or grinding operations processing a separate lead compound. Lead glass complexes obey the laws of temperature elevation, i.e., elevated temperatures will produce lead vapors where degree of vaporization is also related to the chemical composition of the glass. Certain glass complexes chemically bind the component raw materials into higher stability. Our technical staff suggests that high alumina has this property.

Other technical personnel have offered the suggestion that the higher the valence, the greater or higher the toxicity. Apparently this approach to various industrial toxicity problems needs more study and consideration relating to several troublesome compounds.

Much worthwhile progress could be made by the lead producers if they would consider the problems they are trying to solve from a more practical point of view. I refer specifically to a recent attempt to reduce dust by pelletizing litharge. As I understand it, some of the pelletizing binders introduced undesirable properties into the finished glass. In one or two trial runs involving pelletized material about one-half millimeter in diameter, the grinding action of the pellets en route between a plant and our mixing department produced an unusually fine dust which gave us a heavier concentration of dust than we normally experience with untreated litharge. The size of the pellet may not be as important as recognition of the fact that litharge and many other lead compounds do not stay airborne for more than a fraction of a second. One-hundred-mesh material is air-borne longer than 50-mesh material. Also, larger pellets will move in the batch as it is worked in our processing.

I heartily subscribe to the Health and Safety Division of the Lead Industries Association. Since learning of their operations approximately 10 years ago, we have had an opportunity to draw heavily on their advice and counsel. It is a sincere regret that there is not more staff and money to provide the services of the type they supply industry and the public.

Lead compounds provide a more useful glass. Our industry is interested in new markets. I am convinced some new products and markets will require new properties in our product. There is no reason to avoid the use of lead to reach these goals.

CHAIRMAN BOWDITCH: The paper by Mr. Frank will now be discussed under the leadership of Dr. C. H. Hine, who is Clinical Professor of Preventive Medicine at the University of California in San Francisco.

DISCUSSION

DR. C. H. HINE: I should like to reemphasize that the appearance of porphyrins in the urine is not solely diagnostic of lead intoxication, since increased secretion of porphyrin precursors occurs in a number of diseases, most of which involve the liver or the blood, but which may also extend to include mental diseases, diseases of the skin and chronic infections of various types. There are, however, qualitative measures for distinguishing between coproporphyria III, the derivative of most importance to this problem, and other closely related precursors of hemoglobin. Recently, Minden and Thiele (*Arch. f. Gewerbepath. u. Gewerbehyg.*, 16:326, 1958) demonstrated that the number of different urinary porphyrins, as demonstrated by paper chromatography, increases with the increased absorption of lead. If and when more specific analyses are required, these can be accomplished. I do not believe at this time that a discussion of the exact mechanism of the formation of these materials is relevant, since despite considerable research work there are many facts still to be elucidated. However, suffice it to say that as a screening procedure, there is a high degree of correlation between the results of elevation in these coproporphyria values and urinary and blood lead levels. This test is used with increasing frequency today. Its value was recognized by us some 10 years ago, and we have since instructed our medical students at the University of California in its use as an index of lead absorption. It is my understanding that a number of industries use the procedure rather widely.

The relatively large particle size of the glass frits

and the chemical structure of lead with its incorporation as a borate and silicate all mitigate against absorption into the body. Despite these factors, it would be my recommendation that serious consideration should not be given to altering the present threshold limit values of 0.15 mgm M^3, principally on the basis that it would complicate the present analysis, since determinations would be required to indicate the relative percentages of the molecular forms of the different lead compounds. Mr. Frank's studies have, however, contributed further to the understanding of lead hazards, since he has pointed out that air concentrations of lead silicate and borate considerably above threshold limits, when compared with determination of lead excretion patterns and the physical status of employees, have failed to demonstrate any evidence of either frank or subclinical intoxication.

In addition to the responsibility in the field of health protection for its own employees, management has the responsibility for safety of its product under conditions of ordinary use. As Mr. Frank has indicated, ceramic products may contain considerable quantities of lead, and on occasion they have uses which bring them into contact with the preparation or serving of food. It is my understanding that the industry has voluntarily accepted a standard of the quantity of free lead which can be expected to be extracted from container surfaces. In this regard I would like to refer to some experience we had on the West Coast with the import of some improperly glazed and painted dishes from Japan. Analysis showed that the glaze could contain as high as 32% extractable lead, and this was deemed to be a public health problem since it was felt that continued use of dishes with unstable linings could result in ingestion by consumers of enough lead over a period of time to result in illness. This problem has been corrected without any serious mass intoxication. I am sure that due to the efforts of the Health and Safety Division of the Lead Industries Association such problems are avoided in American industry.

MR. FRANK: I want to say just one thing for our industry. Lead compounds give us more useful glaze. Our industry is interested in new markets, and I am convinced that new products are going to require new properties which can be obtained from lead. I have no reason to avoid the use of lead to reach these goals.

DR. BIRK: Is the problem of lead intoxication in children still met quite frequently in the Boston area and the East? We don't see it very often in California.

DR. A. E. BYERS: Our lead poisoning is mostly in children who chew paint on the cheap housing that was put up in the 1870's, 80's and 90's. Much of this is painted with lead pigments on inside trim. At our particular hospital, we see anywhere from two to 15 cases of lead intoxication annually. Very few of them come from any other source. We have an occasional case of a child from the country where an old-fashioned lead-containing ointment has been applied to the mother's nipples or something of that sort, but practically all cases are from the very cheap housing of the period mentioned.

DR. BIRK: Has anyone had any experience with intoxication from water from lead pipes, acute intoxication?

We believe that such a problem occurred when the water supply in the older part of San Francisco was moved. During that time, the lead content increased quite a bit in the water supply in one area, which we thought produced a hazard of lead intoxication. Has anyone else had experience with that?

DR. A. A. HEMKE: Cases in adults still continue from time to time, particularly in rural areas, when water is conveyed to a house from a spring or well in a system of lead pipes. We see cases of that kind from time to time, and then there are also occasional cases seen in new housing developments where the luting of water pipes with lead-containing luting material results, for a period, in a high lead content in the water.

These are rare, but there are in the literature at least two reports of virtual epidemics of this kind in large areas of new housing developments.

CHAIRMAN BOWDITCH: Our discussion has gone rather far afield from the ceramic industry.

Our final paper this morning will be by Dr. Helmuth H. Schrenk, Executive Director of the Industrial Hygiene Foundation in Pittsburgh. Dr. Schrenk will speak on "Hygienic Lead Standards," a very broad subject.

The significance of hygienic standards depends as much on communication as it does on science and technology. The terms hygiene standard, maximum allowable or acceptable concentration, permissible limit, threshold limit and hygienic guides are used interchangeably. Individual interpretations of the figures are certainly not the same. This is partly owing to a lack of understanding of the technical aspects and the purpose of the standards, and partly to the fact that legal or regulatory connotations are inferred. The latter is a particular stumbling block as there is a tendency to use the standards to "prove" that an injury could or could not occur. Only when the purpose and limitations of the standards are thoroughly understood can they be properly utilized and the greatest benefits obtained.

Standards of good practice have been established in many fields. They are based on available scientific and technologic information and the judgment of a group with knowledge of the particular subject. It is obvious that each member of the group will not have initially the same numerical value in mind, and that the final standard must represent a compromise. The figure finally accepted will be a "round number" and not an "exact" figure. Standards must be recognized for what they are, the consensus of a group exercising its best judgment. The figure accepted is not a fixed scientific value, and might just as well have been somewhat smaller or larger.

The purpose of hygienic standards is to serve as guides in controlling the industrial environment to protect the health and comfort of workers. However, the final criterion of the effectiveness of the standard and environmental controls does not rest on analytical environmental data, but on the worker's response or lack of response, which is determined by comprehensive and thorough medical surveillance. The closer the correlation between the environmental measurements and the results of medical examinations the more meaningful the hygienic standards.

There are three interrelated factors which govern the effective application of hygienic standards: (1) the limits of analytical measurements, (2) potential severity of the hazard and (3) reliability of diagnostic procedures.

The wide variations in the levels of air contaminants to which a worker may be exposed make it difficult to obtain an integrated measure of exposure with a reasonable number of samples. The evaluation of the hazard may be good or bad, depending on such variations and the effects that peak concentrations may have on the worker. Hence, the hygienic standard may be more accurate than the analytical data obtained to evaluate it. This limitation of air analyses can be minimized by instituting engineering controls at sources of high contaminant dispersion, thus reducing peak concentrations. The close relationship between the standards and sampling and analysis is obvious.

A safety factor is an essential consideration in establishing a standard. The magnitude of the safety factor may vary greatly depending on our knowledge of the biological action of the substance in question. If the potential hazard is great, if the margin between minor injury and serious injury is narrow, if the injury produced is irreversible, then a greater margin of safety is required. On the other hand, if the margin between the incipient effects and serious injury is large, if effects are readily reversible and good diagnostic procedures available to detect early changes, then the margin of safety can be small. The type of biological action is also important; for example, whether the action is one of progressive systemic effects, narcosis or irritation. It is noteworthy that the present accepted standard of 1 ppm for chlorine and bromine is the same as given in a table published in 1912, whereas values for solvents, such as benzol and carbon tetrachloride, have been greatly reduced.

It should be evident that a figure in a table of standards or limits has no significance per se, and does not define the relative hazard. It has meaning only when interpreted in terms of analytical, toxicological and medical data applicable to each individual compound. If the legal implications and use of limits to support otherwise untenable positions could be eliminated, the value of standards would be greatly enhanced and the establishment of acceptable standards would be much less difficult.

Standards relating to the concentration of lead in air, urine, blood, water and paints are discussed in the following sections.

Hygienic Standard for Lead in Air

Air analyses are specific measurements of the environment, and permit an evaluation of a hazard before workers are exposed. They have a definite advantage over other measurements which depend on some biological response of the worker to the exposure. Another important use of air analyses is the determination of the sources of dissemination, thus directing engineer-

ing control to those points where controls are needed and at the same time serving as a basis for selecting the type of control most desirable. Subsequent to the establishment of control measures, air analyses can be used to check the effectiveness of the engineering measures. Thus air analyses have a unique role in the prevention of harmful or objectionable effects from environmental contaminants.

The value of such analyses is meaningful, however, only when they can be interpreted in terms of potential hazard; hence the need for hygienic standards for the concentration of contaminants in the air. Briefly, hygienic standards for air concentrations are based on laboratory research using animals, and field studies correlating the medical observations of exposed persons with data on the concentration of contaminants to which they are exposed. Limited human experimentation in the laboratory and experience in the use of a standard serve to substantiate its validity or indicate a need for revision. The better the correlation between air concentration and effects, the greater the reliability of the standard.

It is unanimously agreed that the translation of the results of animal experiments in terms of human response has definite limitations. Hence a factor of safety is used and this may vary widely. A standard based on animal data alone is usually considered tentative. Standards based on field studies are, in general, more reliable. But owing to many factors, such as limitations of air analyses (wide fluctuations in concentrations, physical state of the contaminant and number of analyses usually obtained), lack of precise diagnostic procedures and the difficulty of estimating past exposures, these values also are established with due consideration to factors of safety. In other words, using the best tools available, hygienic standards for air concentrations are not highly accurate fixed values, but rather represent levels of magnitude.

Based on the results of an engineering and medical study conducted by the U. S. Public Health Service in a storage battery plant, it was concluded that, "Except for prolonged exposure, it appears that the limit of safety under the conditions encountered in this study is an atmospheric concentration of lead dust or fumes of less than 0.15 milligrams per 10 cubic meters of air." Prior to this, a value of 0.5 mg cu m. had been used by some. Others were of the opinion that 0.15 was too low and that 0.3 mg cu m was more realistic. Nevertheless, since the publication in 1933 of the storage battery report, the hygienic standard for lead has been generally accepted as 0.15 mg cu m. The fact that this standard has been used successfully for about 25 years indicates that it has been a reasonable value. This does not necessarily make it the best choice nor demonstrate that other values of the same general order of magnitude, such as 0.1 or 0.2, might not have proved just as satisfactory. In fact, a standard of 0.2 mg cu m. has recently been adopted by ACGIH and the Hygienic Guides Committee of the American Industrial Hygiene Association.

The main compounds of lead encountered in the storage battery plant were: PbO, Pb_3O_4, PbO_2, and $Pb(SO_4)_2$, and therefore the figure 0.15, previously quoted, must refer to exposure to these materials. However, the figure is sometimes used to refer to "lead" in an all-inclusive manner. The ASA standard is limited to lead and its inorganic compounds, carbonate, sulfate, oxides, nitrate and chloride. While it is impractical and unnecessary to establish individual standards for each lead compound, it is realistic to make distinction between soluble and insoluble compounds in establishing standards for systemic poisons. For example, two standards were established for uranium and vanadium compounds, one for soluble and another for insoluble compounds. This same principle should apply to lead compounds and is presently under consideration by a committee of the American Standards Association.

Another important factor in regard to air concentrations is particle size. The effective dose of lead is that portion which reaches the lungs and is absorbed into the blood stream. This is supplemented by the lead which is retained in the upper respiratory tract, removed by the action of the cilia, and swallowed. Since probably 90% of the swallowed lead is excreted unabsorbed, a large portion of the lead which enters the respiratory tract may not be absorbed if the particle size is large, and the air concentration, which is determined in terms of weight, may exaggerate the exposure conditions. On the other hand, if all the particles are present as a finely divided fume, the effect may be somewhat underestimated.

It is not so much the standard which is finally established, but rather its proper use which is most important. The evaluation of the potential hazard of the environment should be only one facet of a well balanced program, and should be correlated with engineering and medical control measures.

Hygienic Standards for Lead in Urine

In view of the limitations of air analyses and the fact that exposure to lead compounds has meaning only if lead absorption occurs, it was natural to turn to the analysis of biological materials to provide a measure of lead absorp-

tion. Numerous studies have provided much quantitative information on the relationship between urinary lead excretion and severity of exposure, and the analysis of urine specimens is probably the most common procedure for evaluating lead exposure and absorption.

Normal urinary lead excretion varies from about 0.01 mg to 0.06 mg per liter in large samples of a liter or more, and from 0.05 mg to 0.12 mg per liter in spot samples of 50 ml or more. The mean value is in the order of 0.03 mg per liter. Values of 0.15 mg and 0.20 mg per liter have been generally used as an upper safe limit for urinary lead excretion. However, concentrations considerably in excess of these levels have been found in the absence of any significant evidence of lead poisoning. Conversely, evidence of lead poisoning has occasionally been observed with concentrations less than 0.15 mg per liter. As there may be an overlap in the distribution curves of urinary lead levels in unexposed and exposed personnel, a single result has little meaning. Repeated analyses noting trends, and the findings in a group of exposed persons, reveal more meaningful information on the magnitude of the exposure. The higher the level above the normal range, the greater the likelihood that poisoning will occur, but there is no specific level above which it can be stated that poisoning exists. In other words, urinary lead analyses cannot in themselves be used to diagnose lead poisoning, but they are of value when used in conjunction with other data and clinical findings in the evaluation of the significance of the exposure and in the diagnosis of lead poisoning.

As mentioned previously, urine analyses may indicate a low level of absorption even though air concentrations may be high owing to large particle size or insolubility. The reverse of this also may occur. In one instance in which air analyses showed values well within acceptable limits, and the urine values were quite high, it was found that the exposure was from a source outside the plant. Thus the two procedures can be used to supplement each other in evaluating exposure to lead.

In summary, although a standard or limit value for lead has been established, in practice a sliding scale or range is more commonly used. For example, values below 0.1 mg per liter of urine may be considered of little or no significance, values between 0.1 mg and 0.2 mg constitute an intermediate zone, and increasing values above 0.2 mg are evidence of hazardous lead exposure and the need for improved engineering control. Used in this manner, in conjunction with environmental data and medical findings, there need be little controversy regarding a single standard for the concentration of lead in the urine.

Hygienic Standard for Lead in Blood

The concentration of lead in the blood also provides a helpful index of lead exposure and absorption. It also serves as an aid in the diagnosis of lead poisoning by providing definite evidence of lead absorption and is particularly valuable in cases of nonspecific symptomatology. Blood lead determinations have the advantage that the sample can be collected without the active cooperation of the individual, and without the risk of contamination. Blood lead concentrations are less variable than urine values, and in rare instances of kidney impairment reveal excessive absorption where urine analyses would fail to do so.

In general, however, the same principles apply to blood concentrations as to urine concentrations; namely, there is no specific level of blood lead which can be interpreted as indicating that lead poisoning exists. Blood lead concentrations of the order of 0.01 mg to 0.06 mg are considered within the normal range for persons with no industrial exposure to lead. Values between 0.06 mg and 0.08 mg may be considered a transition zone, and concentrations above 0.08 mg are indicative of unsafe exposure and that control measures should be improved, even though no signs or symptoms or clinical evidence of lead poisoning are present. There may be a disagreement regarding the figures given; however, the principle of a sliding scale is certainly valid and as long as the values are used to evaluate exposure and absorption of lead there is no need to place undue significance on a specific figure.

Hygienic Standard for Lead in Drinking Water

The establishment of a hygienic standard for the lead content of drinking water presents a somewhat different problem as the opportunity for control, monitoring and surveillance is not as readily applicable to the general public as it is to industrial workers. Since at least 1925 the U. S. Public Health Service has placed a limit of 0.10 ppm of lead in drinking water, and a water supply may be rejected if the concentration is above this level.

The results of many analyses indicate that the mean daily lead intake of the average North American adult is about 0.3 mg of lead in food and beverages. This same amount is eliminated daily; hence there is an equilibrium between intake and elimination and there is no lead retention. An experiment in which an additional 0.3 mg of lead per day was added to the average normal intake of 0.3 mg, making a total of 0.6 mg per day, resulted in some lead retention. The safe level of lead ingestion in food and drink

appears to lie between 0.3 mg and 0.6 mg per day. The limit of 0.1 ppm (0.1 mg per liter) of lead for drinking water therefore seems reasonable and satisfactory. The level apparently is not hard to meet, as the results of the analysis of drinking water from 36 cities in the United States gave a mean value of 0.011 mg per liter with a range of 0.001 mg to 0.04 mg per liter.

Hygienic Standard for Lead in Paint

The American Standards Association has established "American Standard Specifications to Minimize Hazards to Children from Residual Surface Coating Materials." The standard was the result of action by a subcommittee of a Sectional Committee on Hazards to Children, Z66, organized on March 12, 1953. The scope of activity of the subcommittee was limited to the potential hazards to children such as might come from the handling and use of painted articles, the hazard being from toxicity of coatings chewed off and swallowed.

The standard specifications state that "a liquid coating material to be deemed suitable, from a health standpoint, for use on articles such as furniture, toys, etc., or for interior use in dwelling units where it might be chewed by children (a) shall not contain lead compounds of which the lead content (calculated as Pb) is in excess of 1% of the total weight of the contained solids (including pigments and drier). . . ." This standard is applicable to a specific use, and is the only standard of which the author is aware which limits the lead content of paint. It would appear logical and reasonable to assume that any standard dealing with the lead content of paint, from the viewpoint of a health hazard, would be based on scientific and technologic data and not on the unscientific concept that, simply because a substance is "toxic," its use should be arbitrarily limited. It should be a fundamental concept that a substance can be used if it is shown that its use for a particular purpose is safe, and that it cannot be excluded simply because it is classed as a poison.

Summary

It has been clearly demonstrated that lead occurs in the human body without any adverse effects, and that a toxic response depends on concentration. Satisfactory hygienic standards for lead have been established, and it has been demonstrated that lead can be used safely if the standards are used, and used properly. The establishment of standards is not an objective per se, but rather a means of obtaining an objective -- the prevention of harmful or objectionable effects. The figures given in the standards have meaning only when used by competent persons and interpreted within the framework of the comprehensive knowledge of the biological action of lead. Figures are not a substitute for sound judgment.

CHAIRMAN BOWDITCH: The modest lady who is going to lead the discussion of Dr. Schrenk's paper said that all she cared to have on the program was the word "Consultant" after her name. It is only right, though, that we should say for the benefit of the few here who may not know, that Dr. Mayers was for many years the head of the medical work of the very excellent Division of Industrial Hygiene of the New York State Labor Department. Personally, I know of few people to whom I would turn more quickly for medical advice on industrial lead problems.

DISCUSSION

DR. MAY R. MAYERS: Unfortunately, standards are being used, not exclusively by competent professional people, but by lay groups who, with the best intentions in the world, try to use them for special purposes. This presents some serious problems.

We meet employers, for example, who, in selecting the materials they wish to use, would like to be able to run down a list of safety standards and pick the one with the highest number, on the theory that it is safer to use than the others. They do not appreciate the fact that the way in which they will use the substance, its physical, chemical and biological properties — whether it is a primary irritant, a sensitizing agent or whatever — will make a tremendous difference in whether it can be used safely for a given purpose despite its relative position in the list of safety standards. In some substances there is a wide spread between a safe level and one which is highly dangerous. In others, the spread may be so small that exposure to toxic concentrations is difficult to avoid. And long-range effects are among the matters not easily incorporated in safety standards. It is important, therefore, to educate employers to understand that the materials they wish to use cannot be selected for safety on the basis of their respective position in a tabulation of accepted safety standards. Numbers always have something of an atmosphere of magic about them, which makes them misleading.

Another lay group which tends to introduce confusion into the practical application of safety standards comprises those who wish to legislate them into code rules and regulations for purposes of enforcement. As Dr Schrenk so well pointed out, safety standards provide excellent bench marks and guides for control of the industrial environment. But in routine enforcement of legal requirements, there are many practical limitations to their usefulness. The number of air samples, for example, which can be taken in the ordinary course of law enforcement, is necessarily limited -- sometimes to only one or two samples. This is apt to be inadequate to evaluate the extent and the nature of the exposure, particularly when surges or intermittent exposure are in-

professional people — nor the limitations of laboratory procedures. They must be impressed with the fact that safety standards have meaning only in the hands of professional people who understand their limitations and how to interpret them.

Erroneous use of safety standards is also common in the adjudication of causal relation in claims for workmen's compensation. When a worker's exposure is shown to have been substantially within the limits of the safety standard, as evidenced by subsequent investigation of his exposure, this is apt to be construed as conclusive evidence that there is no causal relation between his illness and the exposure, regardless of the clinical picture or other medical evidence to the contrary. Two errors are involved in such cases. First, it is not always possible to obtain reliable data, after the event, as to precisely what his exposure was in terms of safety standards. Second, safety standards are useful primarily as guides for control of the industrial environment and the protection of the group. When safety standards are complied with in a workroom, the incidence of injury to health is minimized. But most differences between individuals continue to be important here as in every other branch of medicine. A diagnosis in an individual case is a medical conclusion on the basis of medical findings to which information of the occupational exposure makes an indispensable contribution. Safety standards cannot, however, be used per se to make the diagnosis, nor can they determine the question of causal relation.

I would say that the safety standard for lead poisoning has stood up remarkably well over the years. I believe this is due to the fact that there has been a tremendous experience with exposure to lead in humans. Standards based primarily upon animal experimentation tend to be weak because the results cannot be extrapolated to human exposure with any great degree of confidence. Our present lead standards are remarkably sound, in my opinion. There has been discussion here, and elsewhere, of developing separate standards for the different lead compounds, based on differences in their physical, chemical and biological properties. Theoretically, it should be possible to make such distinctions with profit. However, one must bear in mind that every standard is in essence an approximation; and, since there are so many variables involved, I wonder whether it is wise to go into refinements of the basic standard. I wonder also whether lay groups would not be tempted to take such refinements too literally, and so come to regard the numbers in the standards as even more infallible than they now regard the over-all lead standard, thereby leading to even greater misuse.

DR. C. A. HART: My question pertains to standards for drinking water. I am involved now with a patient who was referred to me and who has been under treatment from California to Texas for an illness that is still undiagnosed. She was referred to me by the hematologist. We found she was excreting considerable lead beyond the usual permissible limits.

country, I discovered one thing that intrigued me. That was that someone had suggested to her that she use alfalfa tea. I asked her to bring me some of her alfalfa tea, which she did. I found the alfalfa tea, the brewed tea, had a considerable quantity of lead in it, so then I asked her to bring me some of the tea in the package. She brought me the tea. I brewed the tea. It had no lead. I asked her how she made the tea. She said she was the first one to get up each morning. She went to the hot water faucet and drew water from the hot water faucet and made her tea and drank it. She has been doing that for a long time. This was the brew she brought me which contained about eight-tenths of a milligram of lead per liter of urine. In trying to find out whether there might be any relationship to the drinking water, I asked whether there were any lead pipes in the water line. She said no.

Their home had been built under FHA specifications. Finally, they dug up all of the water pipe and found 12 feet of lead pipe (¾ inch) between the city water main and their property, from the city main to their household supply line, and the first takeoff from the household supply line was to the hot water tank.

She was the first one up each morning, and drank from the hot water tank.

My question is: Is it still the common practice to use lead pipe from a main to a supply line, or are there still lead pipes in modern homes, and is this of any significance?

CHAIRMAN BOWDITCH: We are concerned in the City of Chicago. Unless I am way off base, it is not merely permitted, but required by the City of Chicago that all services, meaning the pipe from the city main to the basement of the building, must be of lead.

MR. CARL WALTERS: It would seem to me, in the various times and occasions that some of us do have to defend ourselves in litigation cases, that accurate, established standards such as have been discussed here would be the one specific defense that we would have, in that it is an actual figure, and that it cannot be overviolated, or rather, it cannot be used by a claimant's attorney.

In so many cases the claimant's attorney can nullify what the expert states by taking an entirely opposite view, by quoting some of the various doctors including Dr. Aub, Dr. Kehoe, Dr. Shilling, Dr. Schwartz and many others.

The attorney merely refers to and quotes, that part of a doctor's text that fits the claimant's complaints. He can, and often does, completely nullify what the expert states.

DR. HAYHOW: I certainly didn't want to give the impression of undervaluing safety standards. I think they are immensely valuable, as Dr. Schrenk so well brought out. Since he covered that area so comprehensively, I have confined myself to pointing out some of the limitations when used by nonprofessional people, unaware of the dangers. I particularly wanted to stress the fact that numbers cannot

be used as a substitute for medical diagnosis in workmen's compensation litigations.

MR. T. C. WATERS: Our state is blessed with medical schools and a very competent Commissioner of Health of the City of Baltimore who is present today, also a very competent State Director of Health. We have before us the consideration of the amendment to regulations relating to the permissible concentrations of materials.

I would like to underline what Dr. Schrenk has said in his concluding remarks, that these particular MAC values should be a guide to industry rather than be mandatory.

I cannot fail to reply to the remarks made a few moments ago expressing what to me is a pious hope about the establishment of these values. It may sound good in a courtroom, but when we come to defend cases and say that we have complied with these MAC values, that turns out to be not too real a defense. It still goes to the jury, and the jury, time after time, will find for the plaintiff.

CHAIRMAN BOWDITCH: We are scheduled to reconvene this afternoon at two o'clock with Dr. Leonel C. McGee as Chairman. In the interim, luncheon will be served at 12:45 in the Gold Coast Room.

THURSDAY AFTERNOON SESSION

November 6, 1958

CHAIRMAN McGEE: I should like to take this opportunity, as a guest of the Lead Industries Association, to express my appreciation for the fine program which has been arranged, largely due, I assume, to the efforts of Manfred Bowditch. I hope that those who are interested in discussing the papers will try to make their remarks to the point. Use the microphone in the center aisle so that you can be heard. Please, again, identify yourself, because otherwise our stenotypist will not know you, and it will be important for the subsequent record that we know who said what.

Our first paper, "The Lead Content of Water from Red-Lead Painted Tanks," will be given by Hervey B. Elkins, Director, State Division of Occupational Hygiene, the Commonwealth of Massachusetts.

For many years standpipes and tanks for water storage have been painted on the inside with red lead paints since, in the past, lead paints have been generally superior to paints containing other pigments.

The presence of lead in drinking water in sufficient amounts to cause intoxication has been noted occasionally. So far as I have been able to determine, the source of the lead usually has been lead pipe, and ordinarily in domestic plumbing. Previously I could have said it had invariably been lead pipe, but Dr. Kehoe pointed out that there have been other causes of lead in drinking water than lead piping. Even such pipe, as a rule, presents a serious problem only if the water is soft and acidic.

During the last war, the question was raised of the suitability of red lead paints in tanks used for potable water. Laboratory studies undertaken by the U. S. Public Health Service indicated that some lead was dissolved from panels coated with red lead paints. As a result of this finding, it was suggested that the use of lead paint in tanks and standpipes used for the storage of potable water be prohibited.

At the request of the Lead Industries Association, a study was made of the lead content of water from several standpipes which had been painted internally with lead paint. This study, which was begun in 1950, has involved analysis of 70 samples of water from 11 different standpipes coated with three different types of paint.

The paints involved were:

1. Red lead in linseed oil, referred to hereafter as Type I. This is the paint which in the past has been mainly used in water storage tanks.

2. Red lead in a phenolic vehicle, referred to as Type IV. This is currently the preferred paint in many quarters, being faster-drying and supposedly more durable than Type I.

3. Lead chromate in a phenolic vehicle, referred to as F. & F. King paint. This paint has been widely used in New England.

Samples were taken from four standpipes immediately after painting. From three of these, samples were subsequently taken at intervals for virtually the entire life of the paint, five, eight and eight years respectively. The largest number of samples was taken from tanks painted with Type IV paint, as Table I shows, because our main interest, especially at the beginning of the study, was in Type IV paint.

Three of the tanks coated with Type IV paint were in New Jersey. The remaining eight were in Massachusetts. They varied in size from 75,000 gallons to 3.7 million gallons. Samples were collected by engineers of the Massachusetts Department of Public Health, by waterworks personnel and by the writer. Most samples were drawn off from outlets adjacent to the standpipe, a few were dip samples, and some were from outlets somewhat removed from the tank.

TABLE I.

Paint	Number of Tanks	Number of Samples
Type I (red lead)	4	6
Type IV (phenolic base)	6	51
F. & F. King (lead chromate)	1	14
None (indoors)		20

Analysis

Since it was desirable to detect very small traces of lead, large samples (400 to 500 ml) were analyzed. The lead was concentrated by coprecipitation with calcium oxalate. This was found preferable to evaporation or direct extraction with dithizone. The determination was made with a dithizone colorimetric procedure. Analysis of knowns indicated complete recovery and an accuracy of ± 10% if the lead content exceeded 0.02 mg/l.

Results

The results of the 90 analyses are summarized in Table II. By far the greatest number of samples contained a negligible amount of lead, less than .006 mg per liter. I have used the terminology of milligram per liter. A small number contained between .006 mg and .010 mg per liter, an approximately equal number contained between .011 mg and .02 mg per liter. Two samples contained between .02 and .06 mg. One of these, containing .06 mg per liter, was taken from a tank painted about one year previous with the Type IV paint, but another taken at the same time had a negligible lead content. There were no samples in the range between .06 mg per liter and .1 mg per liter.

If you will recall Dr. Schrenk's paper, .1 mg per liter is the permissible limit for lead in

TABLE II.
SUMMARY OF RESULTS

Lead Content (mg/L)	Number of Samples: Standpipes	Number of Samples: Indoors
0.000 to 0.005	50	20
0.006 to 0.010	7	0
0.011 to 0.020	3	0
0.021 to 0.050	2	0
0.051 to 0.100	0	0
0.11 to 0.50	0	0

drinking water. We found there were three samples that contained over .1 mg of lead per liter, and less than .5 mg. These samples are all from tanks not in active service, but used in stand-by service.

One of them was from a tank that had just been painted with F & F King paint. The other two were from a tank which had been painted about three years previously, with the Type I paint. Apparently the water in that tank had a very definite lead content.

How can we reconcile these results with the findings of Fairhall and Fraser of the Public Health Service that lead dissolves freely from lead paints such as those used in these standpipes?

The obvious explanation is that the water does not stay in the tank long enough to pick up appreciable amounts of lead. The three standpipes studied most thoroughly were in institutions where the daily water consumption approximated the tank capacity.

We have carried out a few panel studies in our laboratory and, in general, confirm the report of the Public Health Service, that appreciable amounts of lead are dissolved, especially from Type I paint. As a matter of fact, Type I paint with litharge added, which, we understand, is frequently used, gave off appreciably more lead during the first few months than the straight red lead in oil.

Our results, converted to mg of lead dissolved per square foot of surface per day, are summarized in Table III.

TABLE III.
SUMMARY OF PANEL RESULTS

Coating	Lead Extracted (mg/day/sq. ft.) (average)	
	1st 2 weeks	1st 2 to 9 months
Type I and PbO	5.5	0.20
Type I	2.2	0.20
Type IV	0.24	0.10

The first two weeks in which they were tested in water, the Type I paint with litharge gave off an average of 5.5 mg of lead per square foot per day. The straight Type I paint gave off less than half that amount, and the Type IV paint gave off one-twentieth as much. Now if we take the average extraction of lead for the first nine months, we find the rate is greatly reduced, and it amounts, on an average of the first nine months, including the first two weeks, to .9 mg per square foot per day for the Type I paint with litharge added, a little more than half that much for the Type I paint and about a tenth that much of the Type IV paint. Actually, with the Type IV paint, the experiment only ran a little over three months.

If we assume the same ratio of solution of lead from the interior of a given standpipe as was found in the panel experiment, we can compute the rate of water turnover needed to keep the lead content within specified limits. Such calculations for a standpipe 26 feet in diameter and 20 feet high are shown in Table IV. This is a small standpipe (about 100,000 gallons), and represents rather an unfavorable ratio of surface to volume.

TABLE IV.
TURNOVER OF WATER AND CALCULATED LEAD CONTENT

Paint	Time after Painting	Lead Content	Gallons of Water/day
Type I and PbO	1st 2 weeks	0.1 mg/l	55,000
	1st 9 months	0.01	61,000
Type I	1st 2 weeks	0.1	22,000
	1st 9 months	0.01	20,000
Type IV	1st 2 weeks	0.1	1,000
	1st 14 weeks	0.01	5,700

It is seen that even with oil base paints, a daily consumption of less than the capacity of the standpipe will result in a lead content, from the paint, of less than one-tenth the maximum allowable level. With the Type IV paint, a much lower consumption will yield the same results. With larger tanks, a lower turnover is needed to effect an equal dilution of the lead, since the area of the tank walls and bottom is less, in comparison with the volume, than in the smaller tanks. Conversely, with smaller standpipes a higher rate of water turnover would be needed for dilution of the lead.

I do not believe that any of those who object to the use of red lead paint in standpipes seriously think that enough contamination of the drinking water will result to produce a significant number of cases of lead intoxication. The permissible limit of .1 mg per liter provides a substantial margin of safety for the average individual, as it should. And, according to our findings, this level was not even approached in most of the samples, nor would it be in most systems.

It has been proposed, however, that although harmful levels of lead are not produced in the drinking water, any increase at all in lead consumption is undesirable and should be prevented. I can go along with this argument to a certain extent. If all the water consumed by a large population contained lead right up to the permissible level, a careful statistical study might reveal marginal harmful effects to a small number of individuals with occupational or other exposures to lead, since the amount of additional lead intake required to produce intoxication would be somewhat reduced. As the lead content of the water is lowered substantially below .1 mg/l, however, the law of diminishing returns would apply. I doubt very much that any

with one whose water was absolutely lead-free.

There are other much more important sources of lead intake than lead paint in water standpipes. One such source is domestic plumbing. By this I do not mean lead, but modern plumbing with iron, brass and bronze pipes and fittings. We recently analyzed samples of water in our office and in the home of one of my colleagues and myself, taking samples from the faucets and water coolers the first thing in the morning, and later after the water had run for some time. The results are given in Table V.

TABLE V.
LEAD IN WATER FROM PLUMBING

Source	Lead Content (mg/l) Morning Sample	Later Sample
Office	0.054	0.002
House A	0.035	0.000
House B	0.007	0.000

In each case the lead content of the water in the first sample was measurably greater than that of the second, and in two cases the difference was significant. These quantities of lead are insufficient to cause any concern, and anyone who advocated new plumbing in a house because of lead concentrations of this order would indeed be labeled an extremist. But, according to our findings, the lead hazard from paint in water tanks is even less.

Of course, our studies were limited to a relatively small number of tanks, all in the same section of the country. While some unfavorable conditions, notably the softness and acidity of the waters, which were mostly in the pH range 6. to 6.6, favored the extraction of lead, other factors, such as higher temperatures and chlorine content, may be more prevalent in other areas. It is my opinion, however, that the most important factor is the rate of turnover of water in the tank.

It could be within the realm of possibility, in isolated instances, that the water regularly consumed by a given population may have been stored in a standpipe for several days. Such situations, if they occur at all, would almost certainly involve relatively small numbers of people. In such cases it might be that some coating other than Type I paint would be advisable for the interior surface. It is exceedingly hard to visualize a water supply system, with a tank of comparable capacity to that of the tanks studied, where storage could be so prolonged that Type IV paint would be unsuitable, according to our results.

of water from eleven standpipes painted with lead paint. Of 70 samples of water, only three contained significant amounts of lead, and these were from tanks in stand-by service. Tests of the extraction of lead from panels coated with red lead oil paint indicate that no significant quantity of lead will be added to the average water supply by the paint if the average daily consumption approaches the capacity of the tank; and if a phenolic base paint with a red lead pigment is used, a substantially lower rate of turnover is essential to keep the lead concentration below significant levels.

All the evidence available indicates that only under extremely exceptional conditions, if at all, could the use of lead paint in standpipes for potable water be considered inadvisable from the standpoint of public health.

CHAIRMAN LEMUEL C. MCGEE: Thank you, Dr. Elkins. The discussion now will be led by Dr. Herbert E. Stokinger, Chief, Toxicologic Services, Occupational Health Program, United States Public Health Service, in Cincinnati.

DISCUSSION

DR. HERBERT E. STOKINGER: I think we are probably in substantial agreement, although we arrived at the agreement by somewhat different lines of reasoning. I think there is no question that the amount of lead in our drinking water is of significant health concern to all of us.

Presently, the Public Health Service drinking water standards are being revised. This revision is in a downward direction from 0.1 parts per million to .05 parts per million. What is the reason behind this?

As you know, lead is a cumulative poison. It is also an element to which there is no tolerance developed, as with, say, arsenic. The reason for this is not quite clear, but it apparently has to do with the rapid mobilization of the element from bone storage sites.

It has been shown by Dr. Kehoe and others that the amount of lead; that is, the tolerated dose daily, is in the order of .5 mg per day. This is the tolerance dose.

This means that any amount above this value taken into the body and stored starts accumulating and results in effects on the health. Now where are the sources of this material? They are food, water, air and tobacco smoke. Quantitating these contributions from the various sources, Dr. Kehoe has shown in an extensive study that the food of the average person per day taken in is about .32 mg. It may run up as high, however, as .5 mg.

any question but that he had a frank lead intoxication. He continued to have a low-grade anemia from this and also, on one trial of Versenate, excreted large quantities of lead.

From my own experience, I am not sure how high a lead should be excreted in a normal individual. I think this person put out something like 3 mg to 4 mg in 24 hours.

DR. HAMLIN: I would agree with Dr. Johnstone. With this type of exposure you would certainly have to look for some other factor to account for the employee's illness, particularly after the length of time he had been away from work. In our experience we have seen several men who have been subjected to high lead exposure for possibly 25 years, continue working without ever having had a recognizable episode of acute intoxication. However, as they have approached the age of retirement they have displayed symptoms. I can recall one individual who developed a case of what was thought to be intestinal obstruction but which turned out to be paralytic ileus. The man underwent an exploratory operation from which he made an uneventful recovery but never seemed to be able to get rid of his lead entirely. It seems logical that lead stored in the body tissues over the years might eventually produce symptoms of intoxication in certain cases even after removal from exposure.

DR. HARRIET L. HARDY: Dr. Johnstone, I think, would be disappointed in me if I didn't take issue with him. My experience in the 10 years I have been interested in, and searching for, lead poisoning suggests that plumbism has by no means disappeared. I have seen some very dramatic clinical pictures which I think are admitted to hospitals mimicking other diseases and the term diagnosis is missed. I have seen two cases of jaundice from red cell destruction whose lead exposure was well substantiated with Dr. Elkins' help. I have seen a bilateral wristdrop in the case of a house painter who got well when he was removed from exposure and given several courses of intravenous EDTA. I have seen hematological abnormalities with long periods of disability. I have a hunch that the physicians who miss the diagnosis of lead poisoning are not here today. They are the house officers, and they are the internists who haven't yet had teaching in the field of occupational medicine.

Dr. Mayers and I were talking at lunch today about our repeated hope that the house officers, probably more than the medical students, would learn some of the criteria for diagnosis of plumbism that you and I take for granted, and which are common knowledge. Personally, I am convinced there is still a good deal of interesting, true lead-induced pathological change in our midst.

DR. PAUL REZNIKOFF: Just as the general physician or the internist fails to go into the industrial history of a patient, so the industrial physician very often fails to consider the entire medical picture are subjected to lead intoxication. They are examined for some condition such as upper respiratory infection, and the physician finds they have a lot of stippling, and he makes a diagnosis of lead poisoning on the basis of that and some laboratory results which he thinks are a little off color. As a matter of fact, when they are thoroughly examined, we find they are individuals who have Mediterranean parents or grandparents, that they have a perfectly clear-cut case of Mediterranean anemia of the minor type. They do have a relatively low hemoglobin which doesn't bother them, and a lot of stippling, and furthermore we prove by a starch, gel electrophoresis examination that they have increased hemoglobin A2.

These people are labeled forever lead poisoning because of stippling, because some laboratory gave them a report of a slightly high blood or urinary lead content.

I think it is important, therefore, to emphasize the fact that the industrial physician has to obtain a complete history and do a thorough physical examination and think of medical conditions other than an industrial disease, because these are much more common in a workman than industrial disorders.

DR. J. C. AUB: In lead poisoning, you might get prolonged symptoms if you have bone disease which liberates calcium more rapidly than normal. Two of these would be hyperthyroidism and Paget's disease, a disease which comes at about the time these men get lead poisoning and which is missed unless you take a lot of x rays.

DR. J. H. POTTER: Dr. Johnstone has emphasized one important fact in this whole field of chemicals and ill health, the lack of skill of physicians as cross-examiners. Medical cases do not go to litigation where there is a clear-cut diagnosis. They go to litigation when the physician attending the plaintiff does not find it possible to make an ordinary type of diagnosis. Then he relies upon history, and of course, history is based on symptomatology. We have been so long sold on the old pathology idea that a specific disease is due to a specific etiological factor and gives a specific morphological pathological picture that we don't realize we are no longer in that era.

The symptomatology of the incipient effect of exposure to a hazardous chemical is no different from the symptomatology of many other ordinary diseases. Bacterial infections are chemical poisoning, not an eating away of tissue by bacteria. Even some forms of cancer, in which the cancer invades the metabolic aspect of neighboring tissues can be a chemical poisoning. The symptomatology is due to interference with the fundamental cellular processes in the body; interference with key enzymes, those involving oxidation reduction situations, sugar metabolism, the liberation of energy for activity of muscles, the building up of proteins as I mentioned this morning in Borsook's work. So long as these diagnoses are not clear-cut and are made on poorly developed histories and poorly

When there is a clean-cut diagnosis, all I can say is that any manufacturer, any employer, who will fight a clean-cut case should go to a psychiatrist!

CHAIRMAN MCGEE: Would the rest of your discussion wait until the round table tomorrow? Thank you, and others who might like to discuss this further. I am sorry we don't have unlimited time. May I express my appreciation to Dr. Johnstone, Dr. Hamlin and the other discussers?

We have had our batting order arranged possi- disciplines look at lead, why shouldn't the attorney look at lead? Ted Waters, of Baltimore.

MR. T. C. WATERS: I deeply appreciate the brevity of your introduction, Lem.

Dr. Foulger has ably presented the subject that I had prepared a paper on. He touched on practically everything that I intended to talk about. [Laughter] And may I say to him, and to you, that he and I are in complete agreement with respect to the subject matter that he discussed.

A LAWYER LOOKS AT LEAD

By THEODORE C. WATERS, LL.B.

I am simply going to call your attention to some of the responsibilities that rest upon the manufacturers and producers of lead because you are dealing with a toxic substance. There are two particular features that I would like to discuss briefly — one, your liability to the employees who may be exposed to the hazards of lead poisoning, if I may use that term, because that is the way it is described in our compensation statutes; and secondly, to the consuming public. I know those matters have been touched upon by prior speakers, and I simply want to call one or two particular points to your attention.

First, with respect to your employees, or the employees who become exposed to the hazard of lead in your operations. You all know that now compensation statutes are effective in all states of the union, in all federal jurisdictions, and by that method we have removed from the field of common law litigation disputes that may arise between the employer and the employee. In a word, these compensation statutes impose upon the employer the liability as an insurer for those particular matters that have been made the subject of compensation in the statutes.

Your laws are not uniform. They differ with respect to coverage. They differ with respect to the type of injuries that are made compensable. They differ with respect to the requirements of insurance, the benefits that are payable and the administrative agencies that are charged with the administration of the laws, but behind them all there is one common purpose: to provide prompt compensation at the time that the injured employee really needs it for those injuries that are truly compensable under the given statute.

Originally, as you know, they were designed to compensate for accidental injuries. Little by little they have been amended to provide compensation for occupational diseases, and today there are only two states, Mississippi and Wyoming, wherein occupational diseases are not compensable. Again we do not find uniformity with respect to that particular feature because in some states we still have the schedule system, naming the particular disease that is compensable — lead poisoning, for example. Some states don't even provide that. In other states, we have the so-called general coverage laws, and may I make this comment that with respect to the administration of those laws, our commissions and our courts are coming to treat them as health insurance laws whether employers or manufacturers like it or not, and I for one don't like it. They are treating them as health insurance laws and you can get Dr. A, who will testify in a very limited and superficial manner that John Smith, claimant, has a particular occupational disease, and you can get your Red Johnstones and Lloyd Hamlins and Lem McGees and Bob Kehoes and all the rest of the specialists in the field of occupational diseases. I should not have omitted my friend, Tony Lanza because he has testified for me, too, but you get the one statement by some one doctor that John Smith has the occupational disease and in spite of all the testimony — perhaps that isn't a fair statement — but in spite of the weight of the testimony, our commissions are coming to find, and our courts are sustaining that finding, that if there is evidence in the record that the claimant has a disease for which claim has been filed, then an award is made. So those of us in practice for insurance carriers, self-insurers for industry, when we step up to the trial tables, have more than two strikes against us in the defense of that type of claim.

I do not mean to belittle the need for the com-

here have heard me say before, and I now repeat, that if we are going to treat these laws as health insurance laws, let's call them health insurance laws. Let's stop this business of calling them workmen's compensation laws. That in my mind has become a misnomer.

Certainly one thing is true. With respect to your employees, they are justly demanding a safe place in which to work, safe tools with which to work, protection from the hazards of their employment. Furthermore, they are properly and justly demanding compensation for injuries sustained in your employment.

I say to you that in your role as employers there is a definite responsibility to see that those objectives are attained, and in this enlightened age I do not believe that any one will disagree with that statement. If you show me the executive who concerns himself about the health and the welfare of his employees, I will show you the company whose compensation risk and cost are minimum.

It is simply good business on the part of you employers to see that the health of your workmen is properly protected.

I would like to call your attention to these legal definitions that have grown up with respect to the term "injury," because after all, we are now compensating for injuries under the compensation statutes.

There have developed three distinct concepts with respect to injury. First, the inability to earn full wages. That is what we started out with because the statutes pay a percentage of the wage that the employee was earning at the time that the injury occurred. Secondly, the total inability to perform any further work. In other words, total disability. Third, the event of an employee becoming actually incapacitated from performing work in the last occupation in which he was employed. In the administration of these compensation laws they are being treated as damage statutes.

John Smith comes in and has a complaint, and that complaint is not resolved in the best medical opinion. It is based upon the fact that he, John Smith, is a poor employee. The person or the corporation against whom he files his claim is a corporation and has assets, and therefore recovery should be had by him.

"Simple service, simply given," that is what your employees are giving, and I say to you and perhaps it is needless to say, root-praise your relationship to your employees and see that they are properly protected in the particular job that you give to them to do.

Now may I say just a word with respect to the liability to the consuming public? Here, since I or a matter that has already been developed, I will simply touch upon it as it relates to these labeling statutes.

Only recently the Committee on Toxicology of the American Medical Association has recommended the enactment of a uniform Hazardous Substances Act in the several states. Some states have already adopted that particular Act. I don't think we want more laws. I think we need proper administration of the laws that we now have. Are we going to have a federal law dealing with the subject of labeling? Are we going to have 49 state laws dealing with that subject? Are we going to have countless municipal ordinances and regulations relating to hazardous substances?

A hiatus will result; confusion to industry. We have to label this particular product in one manner if we sell it in the City of New York. We have to label it in another manner if we sell it in the City of Baltimore, and so forth. We could go on ad infinitum.

The lack of uniformity with respect to that is a real problem in my judgment. Perhaps I shouldn't tell this. Perhaps I tell it incorrectly, and if I do, I hope that the Baltimore Commissioner of Health is in the audience, with whom I had lunch today. He was talking to me with great pride about a recent statute, a recent ordinance in the City of Baltimore dealing with labeling, and if I am incorrect in that statement, I ask Dr. Williams to correct me. He and I are old friends. We frequently disagree, but that disagreement does not in any way affect our respect for each other — at least not mine for him.

He was talking about this labeling ordinance in Baltimore. He said, "Ted, the City Department of Health is going to send to every child that becomes four months old a copy of this ordinance, giving the substance of the ordinance, and we feel this will protect or prevent lead poisoning."

Well, I said, "Huntington, in the first place, the child at four months can't read that ordinance. In the second place, the mother or father who gets it and reads it will not properly understand it when you speak of a toxic substance. And in the third place, no matter what their understanding may be, they are still going to use the product."

The moral that I mean to develop from that is to caution the members of this Association as to the responsibility that is imposed upon them by the various states, by the various municipal ordinances that have been and are becoming affected, dealing with this particular subject.

If you don't, we will get common lawsuits based upon negligence which are tried in courts before juries. There is no ceiling to the limit that

that jury may return as the verdict against Company A, B or C, and therefore you may well face the most distressing litigation in our common law courts that you can imagine.

CHAIRMAN McGEE: The discussion of Mr. Waters' paper will be led by Mr. Arthur S. Johnson, Vice President of the American Mutual Liability Insurance Company.

DISCUSSION

MR. ARTHUR S. JOHNSON: I want to make this general observation as background material. It is either by good luck or good underwriting or good engineering services that the American Mutual has experienced only 12 alleged lead poisoning cases during the last 10 years. Nine of these were non-disabling, requiring only medical treatment of a few visits to a doctor and very simple medical care. Of the three disabling cases, one was an exposure to some melted lead by a man who seemed rather more sensitive than others. He was not seriously ill, and the compensation payment didn't amount to much.

The second was a welder or acetylene burner working on some painted steel, and this involved a few weeks of disability. Incidentally, I am startled that nobody talked about cutting up painted steel with acetylene torches. It is really one of the prolific sources of lead poisoning. The scrap industry is just cluttered up with it. The final case was an interesting one from the legal point of view. It was an exposure to the hazards in a smelting and refining company. The man had intermittent exposure and very brief exposure. By brief I mean he walked across the premises, but he had nothing to do with lead or lead fumes as such. Exposure was considered insufficient to produce his condition, but the Industrial Commission found in favor, because it was demonstrated that he did have lead poisoning. Their statement was that it is prima facie evidence of occupational disease.

It is the understatement of the day that the compensation laws of the several states are not uniform. If anything could be more chaotic, I can't imagine what it might be. Ted Waters spoke of the compensation laws providing exclusive remedy. Exclusive remedy, I think, is against the employer, and Ted would be the last to suggest that it was exclusive to the extent that no third party action was available.

The favorite sport today, if the laws of the state permit it, is to take compensation, let the compensation carrier subrogate his interest in that amount of money and go after a third party such as the general contractor, another contractor or a supplier under the principle of products liability, which to all intents and purposes has made the injured employee public.

A little word or two about the liberalization of the laws by extending benefits. The concept of injuries being compensable under the statutes had a serious upset during the inflationary period of the last half dozen years. This bears upon the law of indemnity as opposed to the law of negligence. It used to be that three or four or five thousand dollars would settle almost any case, but one hundred or one hundred fifty thousand dollars is common today in these cases. There seems to be some evidence, however, that with the inflationary period plateauing off, the value of money leveling off, it might be safe to predict that the cost of claims would kind of plateau off a little, too.

I was interested in Ted's statement that the original concept of accident had evolved first to encompass the inability to earn wages due to a personal injury arising out of and in the course of employment, and he had two or three categories of development there. It might be a little too simple.

There still remains considerable difference between the personal injury notion as such and the disability as such. I need to labor this a little bit because we may be coming into a period when disability as a measure of loss of earnings or inability to work goes by the board, and the mere fact of personal injury becomes the criterion.

Let's take the popular topic of the present time, deafness alleged to arise out of and during the course of industrial exposure.

The notions vary between the several states that are now playing with that problem, whether the deafness must have accompanying it a disability as measured by a loss of earnings, or deafness as a personal injury in which deafness gets paid compensation. This question of loss of earnings has always been a tough one. For instance, a case of asbestosis a number of years ago was judged to be a permanent and total disability and was compensated as such under the compensation law of the state. The man immediately got another job, still occupies it in apparently good health, and his earnings are in excess of any he earned at the asbestos plant.

I would like to amplify what Mr. Waters has said with respect to management not intending to give lip service by promulgating a procedure and then forgetting it. His remark was that those who established control of lead as an operating policy got their money back many-fold.

Let me express it in just a little different way. It is the intention of our insurance company to be quite willing to insure concerns against accidents and injuries that might be described as the unforeseen events that arise out of operating the business. But to insure business risks, or to insure the inevitable foregone conclusion of lead poisoning cases arising out of flagrant failure to provide a safe place to work is quite outside of our underwriting policy.

It might be helpful to wind up my comments on Waters' paper with this one. It seems to me that it might be well to establish the three criteria which must be met to establish compensability of a case of lead poisoning for which the employer may be responsible under the compensation law. I refer to the legal aspect as it now is understood, not this fantastic one of merely compensating injury.

First, there must be established the fact that

somewhere else, and finally that he has been disabled by the injury or the disease of lead poisoning. That is looking at the classic principle that his disease was sufficient to reduce earning power.

These are the three approaches that our claim-legal people undertake to follow, and the criteria by which they try to establish whether they have a defense of a case or whether the injured employee should be compensated without further ado.

DR. JOSEPH C. AUB: Talking as we have today about lead poisoning gives the impression that it is a common disease. This is hardly fair in this case where the disease has become less frequent and therapy. Improvements have occurred in all categories.

This is as it should be. Because the disease can be handled more intelligently, we must be careful not to discuss it as though it is more prevalent than its real incidence justifies. I think the discussion today has tended to give that impression.

CHAIRMAN MEIGS: Thank you, Mr. Johnson and Dr. Aub. To those who did not have an opportunity to discuss the papers this afternoon, I hope you may have one later on.

FRIDAY MORNING SESSION

November 7, 1958

CHAIRMAN GEORGE M. WHEATLEY: The program yesterday, which was so stimulating and interesting, dealt with the problems of the worker and his health as it pertains to lead intoxication. This morning we will move over to another age group and the child will have our attention, at least for the first part of our program. But before we get into childhood plumbism, there were several points that developed yesterday upon which I would like to comment.

Reference was made to the American Standards Association and the standard it has produced for paint to be used on surfaces or objects commonly exposed to chewing by young children; for example, children's toys, furniture, or room surfaces. I would like to take this opportunity to doff my hat, figuratively, to Manfred Bowditch for the work that he did in developing that standard. I don't believe that many people know how much effort he put into this accomplishment. I know, because I was chairman of the American Academy of Pediatrics' Committee on Accident Prevention, the organization which sponsors the ASA committee which developed the standard. It was his understanding of the problem, his knowledge of the right people to consult, which enabled the Academy of Pediatrics to launch this project. And most important, it was the technical help of Manfred himself, and the secretarial help and backing which the Lead Industries Association gave, which made this standard a reality.

There is also another little item which seems appropriate, another illustration of the sort of behind the-scenes role which Manfred has played in many fields of industrial health.

I have reference to the development of poison control centers. This is something which I expect many of you know about, if only in a general way. These community units provide information on possible toxic products that may be ingested, particularly by children. They have been developed in various parts of the country, largely through the efforts locally of pediatricians, health departments and other groups. There are — or were, at last count — 228 such centers. Actually, the idea for this unique community service was suggested to me by Manfred Bowditch.

About 1952, through the studies of the Committee on Accident Prevention of the Academy, I first became aware of the frequency and circumstances of accidental poisoning in young children. Plumbism, of course, was one of the important problems. Manfred was interested in my description of the usual circumstances of a two- or three-year-old child swallowing some unknown amount of a common household product about whose toxicity the attending physician had no knowledge. In our discussion, he thought the necessary information should, and could, be centralized and made available to physicians. This was the germ of the idea which developed into the poison control center. This occasion affords me the opportunity to acknowledge our debt to you, Manfred.

We have as our first paper this morning, "The Effects of Season and Temperature on Childhood Plumbism," by Dr. Anna M. Baetjer, Associate Professor of Environmental Medicine, The Johns Hopkins School of Hygiene and Public Health, Baltimore.

CHILDHOOD PLUMBISM

By ANNA M. BAETJER, Sc.D.

Review of Literature

The Baltimore City Health Department[1] has shown that lead poisoning in children has a marked seasonal distribution, with almost all of the cases occurring between the months of May and October. Most of the cases in the Baltimore study were diagnosed by pediatricians in various Baltimore hospitals on the basis of clinical symptoms plus a blood level above the normal range, determined by the Health Department's blood lead analytical service. In addition, a field worker from the Health Department visited the homes to determine the source of the lead and to obtain samples of the incriminated material for analysis. Of the 720 cases which the Health Department investigated between 1931 and 1938, the majority occurred among children between one and three years of age and were attributed to pica associated with the ingestion of lead paint. The children came chiefly from families in the lower economic classes who resided in old houses where the interior wood and plaster has been coated with lead paint. This seasonal distribution, which is shown in Figure 1, has occurred every year without exception since the investigation began.

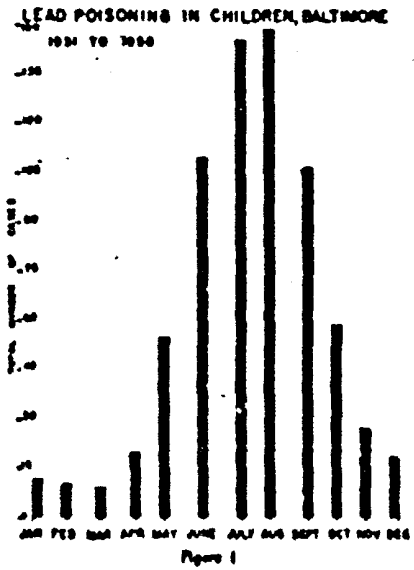

Figure 1

A similar seasonal distribution has been reported for 246 cases in St. Louis,[2] 143 cases in New York,[3] 30 cases in Philadelphia[4] and 21 cases in Chicago.[5] Also, Blackman[6] quotes several Japanese authors as mentioning a tendency of lead encephalitis to appear during the summer and early fall in their country.

In a recent study of childhood lead poisoning, partly supported by the Lead Industries Association, Chisolm[7] showed that although the children reached the ambulatory and teething age at all seasons of the year and thus could be potentially exposed to lead ingestion, the acute encephalopathy did not develop in any of his 32 cases until the first summer following a three-month period of potential lead ingestion. Thus it would seem that the chronic ingestion of lead is precipitated into an acute episode by some factor associated with summer.

In adults this seasonal pattern of lead poisoning is not evident, probably because of the many varying factors which affect adults. Kehoe[8,9] found no accumulation of lead during the summer in his experimental subjects on a high lead intake. Although the concentration of lead in the urine was high in the summer, the total urine lead excretion decreased in association with the decrease in urine volume. The occurrence of stippled erythrocytes increased in summer. On the contrary, Holmquist[10] noted a lower level of stippled erythrocytes in lead-exposed individuals in summer. Hammond[11] reported a sharp increase in the concentration of lead in the urine of lead-exposed workers during extremely hot weather. Since adjustment was made for specific gravity, this increase could not be attributed to a more concentrated urine. Horiuchi and Takada[12] showed that normal healthy persons have a higher blood lead concentration in summer than in winter. Shiels[13] noted a lower incidence of occupational lead poisoning in summer than in winter in various industries in Melbourne, and ascribed this distribution to an increase in lead excretion in sweat during the summer. On the other hand, when he investigated the occurrence of occupational lead poisoning in relation to climate, he found that in persons who were excreting .3 mg lead or more per liter of urine, the percentage who had clinical symptoms of lead poisoning was greater the warmer the climate. Thus the data fail to show any clear-cut trend in adult lead poisoning with season.

The seasonal distribution of lead poisoning in

children has been attributed to various factors. Exposure to the more intense ultraviolet radiation from the sun in the summer and the resulting increase in vitamin D has been the factor most prominently implicated. Shelling and Hooper[14] suggested this theory on the basis that vitamin D increases the absorption of lead from the intestines if the diet contains a high calcium-low phosphorous ratio. Rapoport and Rubin[4] tested this theory in experiments on rats. Animals which were fed a diet containing lead and were exposed to the sun or given supplementary doses of vitamin D daily, lost weight, became ill or died, whereas those given lead but kept in the dark without added vitamin D showed only retardation of growth. Added support is given to this ultraviolet radiation factor by the close parallel between the seasonal distribution of cases and the monthly variation in the intensity of antirachitic radiation from the sun in temperate climates.[15]

Although the increase in ultraviolet radiation may account for the summer peak in childhood lead cases, there are some reasons to doubt that it is the only factor involved. This theory depends on the assumption that these children have a low phosphorous diet and/or lack a normal amount of vitamin D in their diet. Although vitamin D increases the absorption of lead from the gut, Sobel and his co-workers[16] showed that vitamin D had no very marked effect on the concentration of lead in the blood if the diet contained a high phosphorus-low calcium ratio. With prepared milk fortified with vitamin D so widely used by lower income families as a major source of food for their children, a lack of sufficient vitamin D and a low phosphorus intake would not be expected. Furthermore, under some conditions vitamin D increases the deposition of the lead in the bones.

Another explanation which has been suggested to explain this seasonal distribution is that children have more opportunity in summer to chew exterior paints, which generally contain more lead than interior paints. However, data from the Baltimore Health Department surveys indicated that indoor objects are the chief sources of the lead ingested.

The other important environmental condition which has been suggested as the factor responsible for the seasonal distribution of these acute lead poisoning cases in children is the increase in environmental temperature during the summer months. Just as in the case of ultraviolet radiation, the monthly distribution of cases in Baltimore follows very closely the monthly maximum temperature curve. A few investigators have reported an increased susceptibility of animals to some drugs and chemicals with exposure to high environmental temperatures or with a rise in body temperature,[17,18] but only three papers have been found which relate this factor to lead. Blackman[6] showed that rabbits which were subjected to 37°C following a seven-week period of subcutaneous injections of lead, died within 102 hours, whereas those similarly injected but kept at room temperature survived, as did control rabbits at 37°C. The body temperature of rabbits at 37°C rose 3° or 4°C. A seasonal variation in the susceptibility of rabbits to subcutaneous injections of lead was found by Germuth, et al.,[19] the average survival time being much shorter in summer than in winter. On the other hand, Rapoport and Rubin[4] reported that the exposure of rats, which had been fed a high lead diet, to 40°C four hours per day, had no apparent effect on the animals in spite of a rise in rectal temperature of 1° to 2°C.

Experiments on Effects of Temperature on Susceptibility of Laboratory Animals to Lead Poisoning*

Because the ultraviolet radiation theory did not seem an adequate explanation of the seasonal distribution of these childhood cases and because of the few and conflicting experimental data on the effect of environmental temperature on lead poisoning, a series of experiments was undertaken in this laboratory to study the effects of environmental temperature and humidity on the susceptibility of laboratory animals to lead poisoning.

Mice were used in most of these experiments, although rats were tested occasionally to confirm the results on the mice. The two temperature conditions studied were 72°F with approximately 50% relative humidity as the normal exposure and 95°F as the high temperature exposure. In some cases the humidity was kept low in the high temperature chamber but in most of the experiments a humidity of 85% was used. The body temperature of the mice varied considerably in both environments, but the rectal temperature of the mice in the hot chambers did not average more than 1.5°C above those in the normal exposure. In the initial experiments groups of 10 to 20 mice were exposed continuously to the two temperatures for three days before and 14 days after injection with lead. They were injected either intraperitoneally or intravenously with a single dose of lead acetate or nitrate sufficient to cause death in approximately 20% to 40% of the mice at 72°F. In every experiment control mice were maintained at each of the test temperatures. They were injected with sodium acetate or nitrate in amounts

*This investigation was supported by Research Grant RG-4848 from the U.S. Public Health Service. Part of the experiments reported in this paper were performed by Miss Sheila Sumner.

so that the levels of nitrate concentration was equivalent to that in the lead dose. The mice at the 95°F temperature were compared with the mice at 72°F in regard to total mortality during a two-week post injection period; latent period, i.e., time between injection and first death; and the average survival time, i.e., the time between injection and death in the fatal cases. The time of death was taken as the midpoint between the time when the animal was last observed as living and the time when it was found dead. Each experiment was repeated several times and the data were combined for statistical treatment to determine if the differences were significant.

The exposure of the mice to the high temperature increased the mortality significantly, hastened the onset of deaths and accelerated the rate of dying. The effects were more marked when the lead was injected intravenously than when injected intraperitoneally. Since the same results were obtained with intravenous injections as with intraperitoneal injections, the increased susceptibility to lead at the high temperature cannot be attributed to a more rapid absorption of lead from the peritoneal cavity.

The duration of exposure preceding injection of the lead was varied in a series of experiments. High temperature had the same effect whether the mice were exposed only one day before injection or for longer periods up to 30 days, showing that no acclimatization occurred during this period. However, the effect was greater if the exposure to the high temperature began immediately after injection of the lead than when the exposure preceded the injection.

Since children may be exposed to hot days and cooler nights, several experiments were performed in which the mice were exposed to the high temperature for only eight hours each day. The effects of the high temperature were much less under these conditions than when the exposure was continuous. This result may explain why Rapoport and Rubin found no effect of high temperature on lead poisoning in their animals which were exposed to the high temperature for only four hours per day.

In most of the experiments a high humidity was associated with the high temperature. In a few experiments the effects of lead injection were compared in mice kept at 95°F 85% RH with those kept at 96°F 25% RH. The results indicated that humidity was much less important than the dry bulb temperature. This result was not surprising since mice do not sweat.

Because children sweat in high temperature and may become dehydrated, it seemed possible that the seasonal distribution of childhood cases might be attributed to dehydration rather than to the high temperature. Since mice do not sweat this man. Dehydration was produced by restricting water intake leading to a 12% loss of body weight over a three-day period preceding the injection of lead and was maintained for three days after injection. Dehydration significantly increased the mortality at both test temperatures and hastened the onset of deaths at high temperature when the lead was injected intraperitoneally, but had less effect when it was injected intravenously.

After determining that high environmental temperature increased the susceptibility of mice to acute lead poisoning, a series of experiments was performed to study the effect of high temperature on chronic lead poisoning. These chronic experiments probably duplicate more closely the conditions existing in the childhood cases. In these experiments the mice were injected intraperitoneally six days per week with smaller doses of lead nitrate than those used for the acute experiments. Control mice received comparable doses of the sodium nitrate. The mice were kept at normal temperature during the injection period. The injections were continued until the lead group showed a consistent weight loss which was usually between 16 and 28 days after the beginning of the injections. Half of the experimental and control mice were then placed in the high temperature chamber. Mortality was significantly higher and latent time significantly shorter in the lead-injected mice exposed to the high temperature than in those kept continuously at the 72°F temperature.

The physiological mechanism responsible for the higher mortality and the more rapid onset of illness and death in the mice and rats at the higher temperature is not clear. A number of possibilities can be suggested. The increase in body temperature may have increased the rate of chemical reactions in the mice and thus increased the reaction to lead, but the magnitude of the temperature effect was considerably greater than would be expected on the basis of the small rise in body temperature and the usual Q_{10} value of two to three which is characteristic for most chemical reactions in the body. The basal metabolic rate in the mice probably was increased by exposure to the high temperature. Experiments are now in progress to determine if an increase in metabolic rate produced by thyroxine increases the susceptibility of mice to lead. Since the mice at high temperature eat less food and tend to lose some weight, it was thought that these factors might contribute to their greater susceptibility to lead, but experiments performed by McQuary[9] in this laboratory showed that restriction of food intake did not increase susceptibility to lead poisoning. It seemed probable that the mice at the high tem-

perature might be excreting less lead than those at normal temperature. This theory was tested by comparing the urine and fecal lead excretion in rats at 72°F and 95°F temperature. The determinations showed that the animals at the high temperature excreted significantly less lead in their urine over a period of 14 days following the intravenous injection of lead than the animals kept at 72°F. The decrease in the output of lead in the urine was probably related to the lower total urine volume, since Kehoe[8] showed that the urinary lead output per unit of time varied in accordance with the volume of water excreted by the kidneys. The total fecal output of lead was also somewhat less at the high temperature. A number of other experiments are currently in progress to test various other theories which might account for the increase in susceptibility of mice to lead poisoning at high temperature. It is hoped that these experiments will help to explain the seasonal distribution of childhood cases.

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CHAIRMAN WHEATLEY: Thank you very much, Dr. Baetjer. The discussion will be opened by Dr. J. Julian Chisolm, Jr., Assistant Professor of Pediatrics, The Johns Hopkins School of Medicine.

DISCUSSION

DR. J. J. CHISOLM, JR.: May I congratulate Dr. Baetjer on some most interesting observations. I should like first to emphasize what she has said about the role of summer in producing the acute manifestations of lead intoxication in children. Figure 2 depicts the relationship between season, duration of lead ingestion, and onset of acute lead encephalopathy in a group of 32 children. It can be seen that children may ingest lead throughout the winter without apparent illness, but that the advent of summer promptly precipitates acute encephalopathy. These data are well supported by individual clinical histories.

Under Dr. Baetjer's experimental conditions, heat and dehydration certainly do enhance the toxicity of lead. Her experimental conditions require comment in order to determine to what extent this data may be applied to clinical situations. The degree of dehydration produced experimentally in the mice was quite severe; namely, a loss of water equivalent to 12% of body weight. Such severe states of dehydration may nonspecifically enhance the toxicity of a number of agents. This severe degree of dehydration is rarely encountered clinically in acute lead intoxi-

RELATIONSHIP BETWEEN MONTH OF FIRST BIRTHDAY AND MONTH OF INCIDENCE OF ACUTE ENCEPHALOPATHY

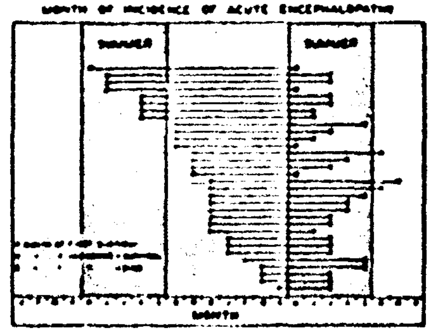

Figure 2

In this graph the month of onset of acute symptoms for each of the 32 patients who developed acute lead encephalopathy prior to 3 years of age is shown on the right. On the left is the month of the child's first birthday. These points are joined by a line. The length of each line, therefore, represents the assumed duration of lead exposure (in months) for each child. Twelve months of age was selected as the average age of ambulation. The nature of the exposure in this series required that the child be ambulatory in order to reach the sources of lead in his environment. In this manner a relation between presumed duration of exposure to lead and the seasonal factor in the production of symptoms can be demonstrated. (Reprinted from Pediatrics 18:362, 1956.)

[illegible]
OF ENVIRONMENTAL SOURCES OF LEAD*

Classification of Patients**	No. of Patients	No. of Specimens	Lead Output (mg./24 hrs.) Mean	Median	Range
Type II and III					
At Home During Exposure	6	16	44.0	27.0	1.04 - 104.0
In Hospital after Therapy	6	[illegible]	0.300	0.240	[illegible] - 0.800
Types I, II and III					
At Home After Exposure	8	[illegible]	[illegible]	[illegible]	[illegible] - 1.00
Type I					
At Home During Exposure	6	[illegible]	2.36	1.21	0.216 - 9.00
Household Controls					
At Home During Exposure	11	[illegible]	[illegible]	[illegible]	0.007 - 1.05

*The household-study group has been divided according to both diagnostic classification and presence or absence of lead exposure, in order that the observed differences in fecal excretion of lead under these varying conditions can be seen. Each specimen represents a 3 to 4 day pooled collection of feces from the lead content of which is calculated the [illegible] lead excreted per 24 hours. An average of two such specimens were collected from each patient during each period of observation relative to exposure.

**Clinical Diagnosis at time of Admission to Hospital:
Type I - asymptomatic increased lead absorption
Type II - acute lead intoxication
Type III - acute lead encephalopathy
(adapted from *Pediatrics* [illegible])

cation. I should be most interested to know what lesser degrees of dehydration may produce in future experiments.

With respect to the temperature elevation produced in the mice I understand that mice are relatively poikilothermic. Human infants greater than three months of age do not exhibit wide fluctuations of body temperature in response to change in environmental temperature as do the mice. Children with acute lead intoxication have normal temperatures unless they experience excessive vomiting or prolonged convulsive activity as a result of their acute lead encephalopathy.

I call your attention to Dr. Baetjer's observation that continuous exposure to high environmental temperature increased lead toxicity in the mice to a much greater degree than did intermittent exposure to high temperature. Differences in heat exposure may explain some of the differences between the results of various workers who have studied this problem.

How do these experimental observations parallel clinical experience in children? They simulate a situation that is occasionally met in children who develop chronic infections superimposed upon an increased body burden of lead. After a prolonged period of continuous fever the acute manifestations of lead intoxication may develop in such a child irrespective of the season of the year. The older clinical literature is replete with such examples. Since the advent of antibiotics, chronic febrile illnesses have become rare in children. Acute lead poisoning precipitated in this manner has likewise become rare.

Dr. Baetjer designed her experiments to bypass the role of intestinal absorption. Clinically, this is a most important factor. Acute lead intoxication occurs almost exclusively during the summer in children actively eating lead. The only recognized exception to this is the presence of febrile illness just discussed. I will present some data to illustrate this important clinical point. These data in Table I were obtained from a group of children all of whom were excreting increased amounts of lead in the feces. You will note that the children who became ill were those who were eating the larger amounts of lead at the time of their illness. When they returned to their homes but were no longer eating lead, no recurrence of acute plumbism resulted, although they were still exposed to the high environmental temperatures of the summer. This abdominal x-ray film (Figure 2) represents a belly full of paint and plaster. The child's blood lead concentration about the 1st of July was .23 mg per 100 gm of blood. Although asymptomatic he was hospitalized to prevent further lead ingestion. He never became ill. We attribute a large part of the improvement in our "therapeutic results" to

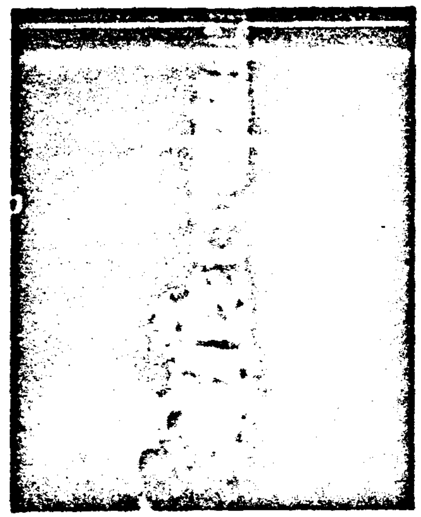

Figure 2

Abdominal x-ray shows large numbers of paint flakes eaten by child. [illegible]

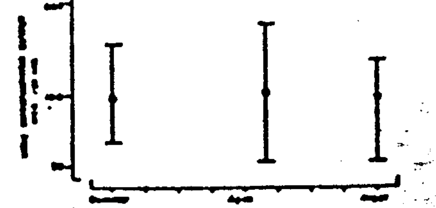

Figure 4

This graph shows the mean and range of serial 24-hour urine coproporphyrin outputs in a group of 15 patients. They had had acute lead encephalopathy during the summer preceding the winter, spring and summer included in this graph. None was ingesting lead during the period of time shown in the graph. All had increased body stores of lead. Urine coproporphyrin output is used as an index of biochemical lead toxicity. Under these conditions no seasonal fluctuation in urine coproporphyrin output is observed.

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removal of patients from exposure prior to the onset of symptoms. Such patients are exposed during the remainder of the summer to high environmental temperature and increased ultraviolet solar irradiation, but they do not become acutely ill.

The studies of Sobel[1] and of Rubin and Rapoport[2] indicate that vitamin D plays an important role, regardless of the diet, in increasing the absorption of lead from the intestine. Sobel and his co-workers also showed that diets producing a low concentration of phosphorus in the serum tended to increase the concentration of lead in the blood. It is of interest that children severely ill with acute lead intoxication do have a low serum phosphorus concentration, apparently as a result of the renal tubular lesion produced by lead.

Finally, I should like to present some observations on the effect of season on children not eating lead. These data were obtained from children who had had acute lead encephalopathy during one summer and were followed during the ensuing winter, spring, and summer with serial measurements of blood lead concentration, urinary coproporphyrin output, and hematologic parameters. These children had an increased store of lead in the body. Figure 4 suggests that urinary coproporphyrin output in this group of 15 children was not affected by season. Figure 5 indicates that a gradual diminution in blood lead concentration occurred independent of season in this same group of children. We concluded from these data that season has little effect upon children not actively ingesting lead.

Studies on the effect of heat, of vitamin D intake and of solar irradiation explain much about the increased clinical incidence of acute lead encephalopathy during the summer months. They do not offer a completely satisfactory explanation for the mechanism by which encephalopathy is produced. There are other possible explanations. One almost totally uninvestigated possibility is the effect of ultraviolet radiation upon porphyrin metabolism. Porphyrin metabolism is grossly deranged in lead intoxication. I should think this offers still another fruitful field for study.

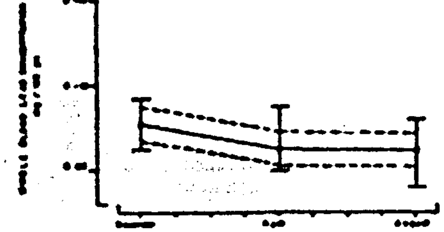

Figure 5

This graph shows the changes with respect to season in mean and range of serial blood lead concentrations in the same group of 15 patients for which data is presented in Figure 4. The environmental conditions are the same. No seasonal fluctuation can be seen; rather, a gradual diminution in blood lead concentration is apparent.

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DR. J. G. FOULKES: I was particularly interested by your last remark, Doctor, about porphyrin metabolism. There is a complete parallel to this situation in poisoning by methyl methacrylate monomer. This substance, in high concentration, interferes seriously with the porphyrin metabolism in animals and produces coproporphyrinuria, and these animals when exposed to ultraviolet light die at a greater rate than in the dark. It is an easy way to produce a porphyrinuria because the compound itself is not very highly toxic. It does affect the liver; so also, to some extent does lead.

Of course, the question of temperature and dehydration and increased metabolic rate is not new. One of our greatest fears in the use of DDT and the possible absorption of DDT by children was that DDT is stored in the fatty tissues, including the brain, and an increased metabolic rate from a fever incidental to thermal efforts or to disease will mobilize the DDT in the bloodstream, causing acute DDT poisoning and death, so you have these two parallels to this lead situation.

It doesn't follow that the cases represent acute poisoning in the summer. That curve, though it looks like a probability curve, may merely be similar to transient in electrical engineering. A steady process has been going on of absorption of lead.

Suddenly something comes along that reverses it.

Now, the fundamental process, if we can accept porphyrinuria as being a very early sign of exposure to lead, may well be the process I was talking about, the interference with incorporation of amino acids and similar compounds into the cells and the accompanying energy factors involved there.

We are dealing with an encephalitis irritation of the central nervous system. The enzyme system of the brain is based particularly upon the oxidation-reduction mechanisms, and the basic material on which the brain feeds is glucose. If one interferes with these systems involved in oxidation and reduction, and certainly the hemoglobin and porphyrin system is one of them, we are seriously endangering the life of an animal or a patient.

DR. HUNTINGTON WILLIAMS: In Baltimore we have a record of more cases of child lead paint poisoning possibly than any other community, seven hundred twenty-four so far reported since we began this war in 1931. One hundred twenty-two of them have died. I saved my discussion on yesterday's papers and will put it all into a very few moments.

The New York City labeling requirement on lead paint was the first. It has been followed in Kansas and Illinois, but when we made ours up, we found we couldn't follow it because it was chiefly directed at places where children can chew. We worded it differently. In one tenement ceiling from which the paint is peeling and falling to the floor, the paint is 16% lead. I call it the stalactite room. A child picked up the flakes of paint, ate them, was made sick and was sent to Dr. Bradley's clinic. Both schools, Maryland and Johns Hopkins, are hard at work with us on this problem in Baltimore.

This house has now been posted as unfit for human habitation and the family is moving out into a housing project because it just isn't safe for that child to go back and keep chewing on this, so a labeling saying that you must not put it where a child can chew it would not cover this situation. A child can't chew off the ceiling. He chews off what is on the floor or on a window sill, usually.

I am sure you have run into this error in diagnosis. I consider the New York situation where a child of two died in 1931 of lead paint poisoning. She was taken to two different doctors and was diagnosed as a virus infection and so on. I saw the clock running out on me, and then she was taken to four different hospitals and there was no diagnosis made. At death the medical examiner decided it was lead paint poisoning from eating paint flakes.

CHAIRMAN WHEATLEY: The next paper, "EUTA Therapy in Persons with Excessive Lead Absorption from Industrial Exposure," by Dr. Lee H. Miller, Kettering Laboratory, University of Cincinnati College of Medicine, Cincinnati, Ohio.

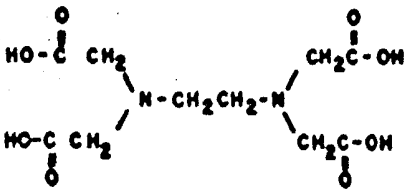
EDTA THERAPY IN PERSONS WITH EXCESSIVE LEAD ABSORPTION FROM INDUSTRIAL EXPOSURE

By LEE H. MILLER, M.D.

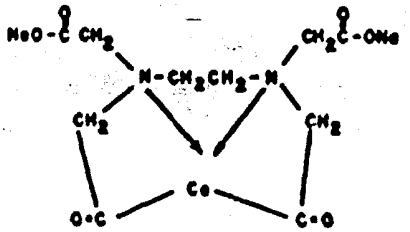
Excessive lead absorption by persons in industry may occur as a result of one or more of the following: inadequacies or failures of existing measures for control of processes in which lead or lead compounds are used; poor personal hygiene; individual or group carelessness or indifference; unrecognized sources of lead exposure; and accidental exposure to readily absorbed lead compounds, such as tetra-ethyl lead.

Because these circumstances still occur with surprising frequency, physicians who are responsible for the health of persons engaged in occupations in which there is exposure to lead, and those who undertake to treat persons suspected of having lead poisoning, must be acquainted with a basic body of information that must include: (1) familiarity with the symptomatology, physical findings, clinical laboratory findings and the natural clinical course of the syndrome; (2) knowledge of the range of the concentration of lead in the blood and urine of persons who have had no unusual exposure to lead, and the significance of deviations from these values when obtained by reliable analytic methods performed by competent, qualified personnel; (3) recognition of the fact that certain findings such as a gingival lead line, an increase in the numbers of "stippled" erythrocytes or elevated levels of lead in the blood or urine are not, by themselves, diagnostic of lead intoxication (4) a practical understanding of the pharmacology of potentially useful therapeutic agents, the indications for their use, their limitations, possible harmful effects and misuse. Items 1, 2 and 3, have been discussed thoroughly elsewhere.[1,2,3]

Since the previous Lead Hygiene Conference, held in 1948, many fascinating contributions have been made in therapeutics. Notable among these has been the introduction and use of EDTA (ethylenediaminetetraacetic acid, Figure 1) and its salts, all of which are "chelating" drugs. Chelation is the term applied to the process whereby a ring-like structure is formed in which a special type of bonding (coordinate) takes place between some of the atoms that form the ring.[4] A multivalent positive ion such as lead or calcium, when incorporated in a ring complex or chelate, no longer retains its ionic properties. A sequestering agent is a compound that reacts with multivalent positive ions and retains them in an unionized state in a water-soluble product. EDTA and its mono and disodium salts, therefore, are both chelating and sequestering agents. When calcium is added, a chelate is formed; therefore, edathamil calcium-disodium (Figure 2) is the calcium chelate of the disodium salt of the acid, edathamil-EDTA.[5]



Edethamil (generic name)
Ethylenediaminetetraacetic acid
(Ethylenedinitrilo) tetraacetic acid
Figure 1



Edethamil calcium-disodium (generic name)
Calcium disodium salt of ethylenediaminetetraacetic acid
Calcium disodium salt of (ethylenedinitrilo) tetraacetic acid
Figure 2

Pharmacology

The administration of EDTA or its mono or disodium salts to the animal organism results in the chelation and elimination of calcium. Because of this mechanism, it is not difficult to produce toxic manifestations with these agents.[6] To avoid the possibility of producing a state of hypocalcemia, edathamil calcium-disodium is used. The administration of this compound, in lieu of the acid or its mono or disodium salts, does not prevent the removal of lead from the body fluids, and indirectly the soft tissues, since it proceeds to replace the calcium in the ring because of the greater stability of the lead

EDTA complex. The newly formed lead complex is highly soluble in water. Since the lead in the chelate is bound firmly and is no longer in an ionized state, it does not exert its characteristic toxic effects. It is apparent at this point that these properties of edathamil calcium-disodium meet some of the specifications for a suitable or ideal therapeutic agent of this type; for example, the end product should be water soluble; it should be stable and not readily broken down by metabolic or other means within the body; it should be excreted rapidly; it should, for the sake of convenience, be effective when administered orally, and be readily absorbed; and finally, it should be relatively nontoxic when administered in effective amounts over prolonged periods of time. The latter includes the effects that might be induced by the depletion of trace metals that are necessary for the functioning of enzyme systems and other biologic mechanisms within the complex animal organism.

It has been demonstrated that edathamil calcium-disodium is quickly and widely dispersed throughout the soft tissues and fluids after intravenous or intramuscular administration, and that it is not concentrated significantly in any organ.[7] The compound does not appear to enter the cellular components of the blood, and the level in the spinal fluid is far below that found in the plasma.[8] After parenteral administration of the drug, excretion occurs rapidly, primarily via the kidneys. It was found that over 50% was eliminated from the body within the first hour, while 90% was removed within seven hours. The absorption of the drug from the alimentary tract is delayed and relatively poor. Evidence of renal damage has been observed in humans and degenerative changes in the tubules of the kidneys have been produced in animals when relatively large doses were administered over prolonged periods of time.[9,10]

The primary "deleading" action is apparently accomplished by removing the lead from the plasma and other body fluids. Shortly after the intravenous administration of a dose, the levels of lead in the blood may rise[11] without producing adverse effects. The lead level then falls, as excretion of the complex proceeds. Subsequently, the lead content of the blood may increase appreciably, and it may attain very nearly to its original high level, as the lead in the skeleton tends to come into equilibrium with the body fluids and indirectly with the soft tissues of the body. Following upon the administration of the chelating agent, the rate of lead excretion is increased greatly, reaching a peak soon, and then tapering off somewhat as the administration of the chelating agent is continued.

The recommended maximum dose for administration intravenously for each 10 pounds (4.5 kg) of body weight is 0.17 gm per hour, 0.83 gm per day, or 1.67 gm per week.[8] The drug should be given, in a concentration not to exceed 3%, in normal saline or in a 5% dextrose solution. The maximum dose per course of treatment is 2.5 gm for each 10 pounds (4.5 kg) of body weight. Courses should be separated by an interval of seven days, and it is inadvisable to exceed two courses, until or unless analytical results demonstrate a clear need for further therapy. Such need exists when the concentration of lead in the blood fails to diminish satisfactorily, or fails to remain well below a dangerous concentration. All persons undergoing therapy should be checked frequently for evidence of renal damage.

EDTA and the Prophylaxis of Lead Intoxication

The routine, frequent or infrequent, use of edathamil calcium-disodium, or other present or future drugs, as prophylaxis against the absorption of excessive quantities of lead cannot be condoned. As has always been true in the past, prophylaxis can be achieved safely only by controlling the sources of exposure to lead by the application of proper measures of industrial hygiene. The attitude that this cannot be accomplished generally in industrial operations reflects either ignorance of the true facts or an unwillingness to correct unsafe conditions. (There are exceptions which result from the brevity of certain operations or the occurrence of unusual or unforeseen conditions.) In the occasional circumstance where this is not practicable, strict adherence to recognized and properly supervised personal protective measures in conjunction with provision for adequate sanitary facilities, insistence upon good personal hygiene and sound medical supervision of the workers, will prevent the development of cases of lead intoxication.

Quite apart from the fundamental philosophy that prophylaxis should be attained by control of the environment, there are other valid reasons for not employing edathamil calcium-disodium as a preventive measure. First, the toxicologic potentials of the drug are not fully understood. The toxic effects observed in humans and animals from relatively short periods of administration have been mentioned; however, the effects that may be produced by the administration of even low doses over prolonged periods to humans are not known and are matters for conjecture. Second, since this drug is absorbed poorly from the gastrointestinal tract, it is unlikely that the additional quantities of lead that may be eliminated by its use would be sufficient

amounts of lead that are absorbed and retained during exposure to potentially hazardous conditions. Third, the administration of the drug may mask the symptomatology of mild or early lead intoxication, thereby preventing the recognition of hazardous exposure before a more serious or prolonged illness is produced. Fourth, while under the effects of the drug and for variable periods of time thereafter, the levels of lead concentration in the blood and urine are meaningless and may be misleading for diagnostic and medicolegal purposes. Finally, the use of such agents, regardless of their efficacy, tends to lull those persons responsible for the health of the workers into a false sense of security which, invariably, is accompanied by a relaxation of recognized procedures and control measures. Such action, sooner or later, is bound to have serious consequences for all concerned.

Edathamil Calcium-disodium and Lead Intoxication

The objectives of therapy in all cases of lead intoxication are to treat the acute episode and to assist the individual to return to his optimum level of health in the shortest time possible. Paramount to both objectives is the immediate termination of exposure to lead. With edathamil calcium-disodium, it is now possible for short periods of time to effect safely the elimination of appreciably greater quantities of lead than heretofore.[12,13] While this is highly desirable, the extent to which this modifies the ultimate clinical course of the disease cannot be stated with certainty. Dramatic subjective improvement shortly after the institution of treatment has been reported in cases of poisoning from inorganic lead. In other cases, however, symptoms have persisted and have necessitated the employment of additional time-proved measures such as the administration of calcium gluconate intravenously for their relief. Other favorable responses, such as a sharp decrease in the numbers of "stippled" erythrocytes in the blood or in the concentration of coproporphyrin in the urine, have been reported frequently.[11] Some of the claims of subjective improvement in mild cases have been over enthusiastic in all probability, since it is known that this occurs quite frequently soon after withdrawal of the patient from the exposure. It has been noted by a number of observers that, following a course of treatment, the lead in the urine returns to levels of the same general order of magnitude as those found prior to treatment. This is not surprising since it has been shown, in carefully conducted long term experiments, that there is a definite relationship between the length of the exposure and the period of time over which increased after the exposure has ceased.[14]

Edathamil calcium-disodium has been used in patients with tetraethyl lead intoxication.[15,17] As in the cases of intoxication produced by inorganic lead, the administration of the drug resulted in a definite increase in the excretion of lead in the urine. No definite significance could be attached to transient periods of clinical improvement that occurred in association with the increased elimination of lead, since periods of improvement and exacerbations are characteristic of that illness. It is of some importance, however, to note that no untoward effects of the application of this therapy have been observed.

In conclusion it may be stated that edathamil calcium-disodium is a drug capable of forming a chemically inert lead-complex that is rapidly eliminated from the body. At present, it is believed the drug is most useful in treatment of the acute phase of the illness. It is likely, however, that its principal virtue lies in its ability to expedite elimination of potentially toxic quantities of lead from the body. By this means, one may hope to shorten the period of disability or unemployment of the industrial workman. The body of knowledge concerning its useful application in cases of intoxication from lead and other metals is growing steadily, and it is hoped that its true value in lead poisoning therapy will soon be established.

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CHAIRMAN WHEATLEY: We will continue our discussion of EDTA therapy. The next paper is by Dr. Hugo D. Smith, of the Department of Pediatrics, The Children's Hospital, Cincinnati, Ohio, on "Lead Poisoning in Children and Its Therapy with EDTA."

LEAD POISONING IN CHILDREN AND ITS THERAPY WITH EDTA

By HUGO DUNLAP SMITH, M.D.

Since lead poisoning among children is a consequence of the production and distribution by man of certain chemical products, theoretically it should be entirely preventable. Nevertheless, the illness continues to occur with devastating results. In Cincinnati, during the first 10 months of 1958, 20 instances of excessive absorption of lead by children were documented, with four deaths reported. To introduce this topic and to show the fulminating consequences of the ingestion of lead, we shall relate the story of one of our recent patients.

Elaine C. had always appeared to be a pretty little girl, with a big yellow bow in her hair and a full life before her, until early in September, at age two and a half, she began to vomit, and became quite lethargic. After one day of these symptoms her alarmed parents took her to the Emergency Room of the Cincinnati General Hospital.

The physical examination demonstrated that Elaine was drowsy and markedly pale. Her liver and spleen were each slightly enlarged. A careful neurologic examination revealed only questionable increase in her reflexes. Sensitized by the knowledge of the high incidence of plumbism among children in Cincinnati during the preceding months, an alert resident physician proceeded to obtain a blood count and smear, a urinalysis, and x-rays of the child's abdomen and wrists. While awaiting the results of these studies, he questioned Mrs. C. about Elaine's oral habits and obtained the history that ever since Elaine had learned to walk the previous fall, she had been chewing on bits of plaster pulled from a broken area of the kitchen wall. Although Mrs. C. had not thought this behavior to be harmful, she had tried quite vigorously, but fruitlessly, to arrest the habit.

When the results of the laboratory studies indicated a moderately severe anemia with basophilic stippling of the red cells, the presence of albumin, sugar and coproporphyria in the urine, dense lines of radio opacity at the ends of the long bones of the forearm, and large amounts of radio opaque substances in the intestinal tract, a presumptive diagnosis of lead poisoning was made and the child was admitted to the pediatric ward shortly after midnight.

In order further to evaluate the possibility of lead encephalopathy a spinal puncture was performed and the cerebrospinal fluid was found to be under mildly increased pressure equal to 200 mm of water, but to contain no cells. Therapy was begun immediately. Enemas were given to remove as much lead-containing material as possible from the intestine, and therapy with calcium EDTA was started by slow intravenous infusion. It was 3:30 a.m. when the weary intern tumbled into bed, virtuously vain about his skill in aborting the ravages of pediatric lead poisoning. Alas, he did not sleep long, for at 6:15 a.m. he was notified that Elaine's breathing had become slow and irregular, with frequent periods of apnea. A check showed that her pupils were now dilated and unreactive and a repeat lumbar puncture revealed that the spinal fluid pressure had risen precipitously to 500 mm of water. It was obvious now that severe encephalopathy was present.

Following a hurried consultation with neurosurgeons, it was decided that the only hope of saving the girl's life rested upon immediate relief of the cerebral hypertension. Past experience had shown that the use of hypertonic glucose or sucrose solutions* brought only transient improvement followed by further increase in the brain swelling, and that efforts to relieve the pressure by means of repeated spinal punctures were both inadequate and fraught with serious risk of sudden death. Accordingly, with the hope

*To date we have not had any experience using 30% solutions of urea. In other centers considerable enthusiasm exists for the drug.

of decreasing cerebral tissue anoxia consequent to the encephalopathy, the child's temperature-regulating center was paralyzed by pharmacologic methods and her body temperature lowered to 90° F. Thereafter, she was hurried to the operating room where a radical decompression of her brain was accomplished by the removal of almost all of her skull, except a narrow strip of bone down the center overlying the sagittal sinus. Prior to the operation, the child's breathing had become so infrequent that artificial respiration had been required throughout the operation and afterwards she was placed in a Drinker respirator. In addition to the previous therapy with Versene and hypothermia, anticholinergic drugs and a slow gastric drip of skimmed milk were initiated to prevent the development of a so-called "Cushing's Ulcer," and a constant bedside watch was begun. Nevertheless, four hours following the conclusion of surgery and only 20 hours after the child's arrival at the hospital, the heart beat ceased and she was declared dead. The results of the analytical studies for lead are recorded in Table I.

TABLE I.
POSTMORTEM TISSUE ANALYSES FOR LEAD

Blood	0.44 mgm Pb/100 Gm
Liver	8.21 mgm Pb/100 Gm
Vertebrae	14.56 mgm Pb/100 Gm
Femur	21.60 mgm Pb/100 Gm on ash

Were this an isolated or unusual case history our narrative might stop here, but regrettably this is still an all too typical picture. Some two weeks following Elaine's death, our clinicians and pathologists reviewed her case. We should like to report some of the conclusions brought out in their discussion.

As already mentioned, lead poisoning among children remains a serious menace. Its reported incidence in any locale reflects primarily the interest and awareness of physicians and the ready availability of analytical studies for lead. As an illustration of this fact, the graph (Figure 1) depicts the incidence of pediatric plumbism in Cincinnati, where we are indeed fortunate to have available the facilities of the Kettering Laboratory. It may be noted that during the years 1941 through 1948 only eight cases were diagnosed. In 1949 the incidence rose, but we were not yet alerted to the disease, for three of these eight cases had been erroneously thought to be poliomyelitis, and it was only upon postmortem examination that the correct diagnosis was made. This experience jarred us violently and, as can be seen, we soon found that the disease was quite prevalent.

Further evidence of the incidence of this disease was thrust upon us this past summer by the discovery of evidence of absorption of toxic amounts of lead as a coincidental finding in two children with other major disorders. In each instance some one clinical finding common to both plumbism and to the other disease led to the obtaining of blood for analysis for its lead content. Bradley and his colleagues have similarly shown that many unrecognized cases of lead absorption in potentially toxic amounts exist in certain segments of the population. They obtained blood specimens from 333 children in clinics in the socioeconomically deprived sections of Baltimore and in 44.4% there was evidence of dangerous absorption of lead.

The map of Cincinnati (Figure 2) shows that a relatively small area of the city contributed almost all of the cases of lead poisoning between 1940 and 1957. The involved areas are the tenement sections. Furthermore, as urban redevelopment has forced the destruction of old homes in one area, the more recent cases have come from a region which, not too many years ago, festered the four hundred. No new paint has been added to these homes; instead, the explanation for the appearance of saturnism is the fact that the paint has been allowed to crumble and peel; that less well informed families now live in the area, and that socioeconomic conditions frequently prevent sound child rearing. Thus, even though modern household paints may be essentially

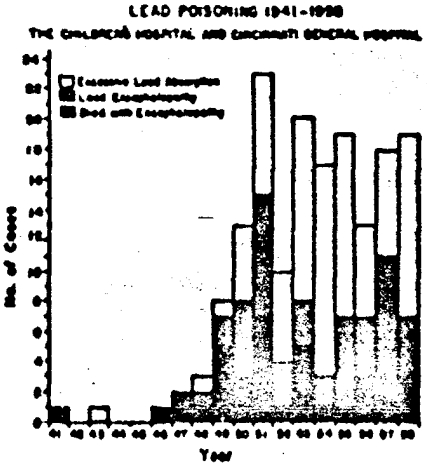

Figure 1
The incidence of lead poisoning, lead encephalopathy and death from lead poisoning seen at the Cincinnati Children's Hospital and the Cincinnati General Hospital 1941-1958.

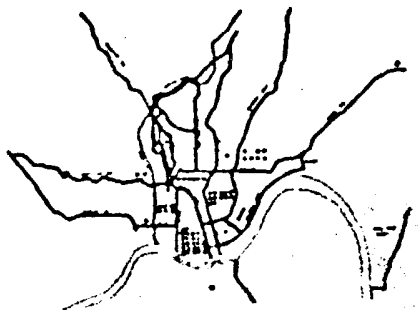

Figure 2
A map of Cincinnati, Ohio, indicating the location of homes of pediatric patients with lead poisoning seen between 1960 and 1967. Of note is the intense concentration in the downtown basin area. Urban redevelopment in this district has resulted in the more recent cases coming from the region in the right center of the city.

lead-free, the threat of childhood lead poisoning will remain a public health problem for many years to come.

Before turning to therapy, we wish to stress a few of the clinical differences between childhood and adult plumbism. The typical findings in adults of peripheral neuritis, abdominal colic, and lead lines along the gums are all quite rare in children. Abdominal pain does occur with considerable frequency, but it is not so severe as to cause the child to double up or to have a board-like abdomen. Associated with the pain are intermittent vomiting, anorexia and constipation. The major concern of pediatricians is the high incidence of encephalopathy, which occurs in about one third of all childhood lead poisoning.

In the management of any child found to have absorbed potentially toxic amounts of lead, two problems must be faced regardless of the presence or absence of signs of actual intoxication: the immediate removal of as much lead from the soft tissues as possible, and the prevention of re-exposure to lead. For the former problem, calcium disodium EDTA or Versene is the accepted drug of choice, but therapy with it is far from ideal. Numerous studies have shown that the initial course of EDTA given intravenously removes only a small per cent of the total body lead and not even all the lead in the soft tissues. On the average, only 25 mgm of lead is cleared by the first course and four or five days' time is required for this. Accordingly, in most instances we give at least two courses of therapy and at times many more are needed before safe levels of lead in the blood ensue.

Oral therapy for children seems unwise with rare exceptions, for not only is Versene by this route less effective in removing lead from the body, but also it is frequently difficult to be certain that the child's exposure to lead has ended. A further problem we have met is the exacerbation of cerebral symptoms in the first 24 to 48 hours following the initiation of parenteral therapy with EDTA. To date, a change to the subcutaneous or intramuscular route of administration with efforts to limit the volume of fluid given has not resulted in a clear-cut improvement in our results. We are now recommending a more gradual onset of therapy, beginning with 25 mgm of EDTA per kg of body weight over the first 24 hours and then, if all goes well, increasing to 75 mgm per kg per 24 hours for four more days. It should be stressed that Versene is not a curative drug, but serves only to lower the amounts of lead in the body more rapidly than occurs by natural processes. Therefore, Versene alone cannot be considered as adequate therapy, especially for the more threatening manifestations of lead poisoning.

Efforts to prevent further exposure to lead are also confronted with difficulties, the major of these being that the causes for pica are not fully understood. To be sure, in many cases, psychiatric abnormalities in the child or disturbances in his environment can be uncovered and because of these we routinely seek the assistance of our social service department. However, attitudes cannot be changed overnight and economic deprivation often defies correction. Although a moderately severe iron deficiency anemia is almost universally found, therapy with iron has not been of much value in aborting the pica, even though the anemia is relieved. Accordingly, as in other forms of lead poisoning, preventive efforts must be based upon removing the source of exposure. To this end, the labors of the health departments have been of considerable value once a case of plumbism has been reported. However, little has been done to correct dangerous situations before poisoning has occurred, in spite of our knowledge of the epidemiology of the disease.

When the disease has progressed to the encephalopathic stage, a real threat both to the brain and to life exists. The marked swelling of the myelin tissue within the rigid bounds of the skull results in extreme increases in intracranial pressure and in compression of the blood vessels supplying the brain. The integrity of the brain cells is thus threatened by anoxia, as well as by possible direct enzyme poisoning by the lead. In an effort to decrease cerebral metabolism and thereby to minimize any cerebral metabolic deficit of oxygen or other nutrients, we

in the vicinity of 90°F to 91°F, through the use of ice packs plus pharmacological methods of paralyzing the temperature-regulating centers. Despite therapeutic failures in several of our initial attempts with hypothermia and despite the fact that this form of treatment does increase the complexity of fluid therapy and may retard the removal of lead, we believe the procedure is sufficiently simple and carries adequate theoretical reasons for causing improved results to justify further trial.

When, in spite of other therapy, the cerebral spinal fluid pressure continues to rise and when dangerous consequences of such pressure develop, such as irregular respirations, apnea, marked bradycardia, papilledema or prolonged seizures, then radical cerebral decompression has been resorted to as a life-saving measure. The results reported by McLaurin and Nichols (Table II)

TABLE II.
RESULTS OF THERAPY WITH RADICAL DECOMPRESSION*

	Encephalopathy	Died
Prior to decompression therapy	[illegible]	[illegible]
Since decompression therapy:		
a) total	[illegible]	[illegible]
b) treated by decompression	7	[illegible]

*McLaurin & Nichols: Pediatrics 20:653, 1957.

indicate a definite decrease in mortality following the introduction of this method of treatment, but unfortunately only life and not brain function appears to have been spared. We have frequently urged earlier neurosurgical intervention, preferably before major signs have developed. However, this procedure is of such a drastic nature that one can easily understand how reluctant a neurosurgeon might be to undertake it with only minimal indications. The therapy of acute encephalopathy accordingly remains unsatisfactory and again we must urge that prevention rather than cure be our first line of defense.

In conclusion it should be stressed again that lead poisoning continues to be recognized with disturbing frequency in cities which are alert to the disease and equipped to provide analytical analyses for lead; that the source of the lead nowadays is paint which was applied some years ago and which has been allowed to fall into deteriorated states; that the illness primarily involves one to four year-olds, and strikes almost entirely in the summer months; and that the disorder is virtually confined to the socioeconomically deprived slum areas. It should further be stressed that specific therapy has not met with great success once intoxication, and especially encephalopathy, have occurred. EDTA therapy, lead compared to the total in the body. Accordingly, the major effort in childhood lead poisoning must continue to be to prevent exposure. The responsibility for this effort should rest primarily with our public health departments.

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CHAIRMAN WHEATLEY: The discussion of Dr. Miller's and Dr. Smith's papers will be opened by Dr. Harriet L. Hardy, Associate Physician, Chief, Occupational Medical Clinic, Massachusetts General Hospital.

DISCUSSION

DR. HARRIET L. HARDY: How is a diagnosis of childhood plumbism made at postmortem if the diagnosis is not suspected? I ask this out of interest in the problem of porphyrin metabolism. Dr. Maloof and I have often wondered if one demonstrated porphyrin in fresh postmortem tissue in the central nervous system, possibly explaining some of the symptomatology in adults such as lead colic.

I would like to ask Dr. Smith to push the idea that it is important to immediately remove as much lead from the soft tissue as possible. Isn't the problem rather to remove the lead from circulation? Isn't this the lead that is harmful?

Also, I wonder if he isn't too discouraged about not removing all of the lead. If one could stop the exposure, it seems to me that one need not get discouraged about a number of courses of calcium EDTA. We have thought that when the soft tissue lead is removed with this drug and the drug is stopped, the lead comes from the skeleton into the soft tissue, and this can be repeated again and again with the judicious type of therapy that both Dr. Miller and Dr. Smith have been emphasizing.

I remember a case we had on the metabolic ward at Massachusetts General of an adult storage battery worker with acute lead poisoning, and we gave him EDTA every day consecutively for a whole month. He got to the point where he was excreting pretreatment levels of urine, but if we rested him from the drug for a day or two, then the lead ex-

into the soft tissues. Surely this is all still somewhat mysterious; the body has stored the lead away to prevent it from producing toxic effects. Yet the exacerbation of cerebral symptoms 24 to 48 hours after the beginning of EDTA that Dr. Smith has been telling us about, Dr. Byers tells me he has little evidence of on children. It is certainly not seen in adults to my knowledge. Apparently Dr. Miller hasn't seen it. Could the rate at which the drug is given be important?

Dr. Lamb, who has had a lot of experience with this drug in bringing down high blood calcium levels, has suggested from his toxic effect experience that this has to do with the rate at which the drug is given, but perhaps the best thing to say is that it is a difference in vulnerability of the central nervous system of the child and adult.

I was very much interested in Dr. Smith's use of hypothermia. It seems to be a highly intelligent move. Does he keep on using the calcium EDTA at the same time in view of what he told us about the exacerbation of cerebral symptoms?

I think all three of us are agreed that oral EDTA is only to be mentioned to be condemned, and I won't go into the reasons. That has been well done.

Certainly the three of us agree that in situations of acute toxicity, EDTA is highly useful.

I think it is important to mention now that the rate of exposure must be crucial in deciding acute effects, particularly in the adult. I think the childhood problem has been so well gone over by others that I won't mention it, but my clinical experience suggests that the body has a fantastic ability to handle lead if it isn't presented with the lead too rapidly, and this rate at which the lead is presented to the body must have a lot to do with the differences in clinical course and experience that Dr. Belknap reported yesterday and in the few cases of Pb poisoning which I described briefly in earlier discussions. So there is no question but that we would all agree that judicious use of EDTA for acute cases is surely the best treatment.

Chronic toxicity, by which I mean the result of exposure to low levels, above permissible level exposure of lead over a long period of time with laboratory evidence of lead effect plus illness, this situation in my opinion, Dr. Miller, calls for the judicious use of short, slowly given courses of CaNa EDTA. We have been very much impressed with the porphyrin and hemoglobin abnormalities returning to normal with such treatment. I feel no hesitation in the wisdom of suggesting this, the routine being done over and over again.

I would like to talk briefly of something we have been doing. That is to use a single dose of calcium EDTA intravenously diagnostically. I think this may have real merit.

We showed that three adult volunteers from our staff at the General Hospital excreted from an average of .06 mg of lead per liter up to 5 mg of lead per liter with a single dose of 1 gm of EDTA intravenously. This is a rough base to work from.

cases, and one gets a tremendous really important increase in urinary lead excretion and this can be corroborated with one or more signs and symptoms of lead intoxication, then the diagnosis of harmful lead effect is made. This strikes me as being an appropriate diagnostic maneuver carrying very little, if any, risk.

Yesterday I was listening with interest to the repeated assertion that we no longer have epidemic groups of cases of industrial lead intoxication. There is no question about this, but we have still got a group of important cases that need to be studied. I think they are missed, and they are incorrectly diagnosed sometimes if lead is not a suspected etiology. They are often impossible to diagnose. There is a nonspecificity to many lead caused signs and symptoms.

Because of such nonspecific syndromes mimicking other diseases, I would suggest to this group that you consider the use of EDTA in single dose for diagnostic purposes.

I would like just to mention the fact that the complexing agents are certainly here to stay.

Kety and Letonoff, I think, get credit for suggesting this earliest. We have the reports of Shubert, Foreman, Lamb and others, and now that we are in this brave new world of ours, where there will be inhalation of heavy metals of toxic potential, this expansion of knowledge of chelating agents I think is very important. The list below shows a few new chelating agents which I culled out of the literature: Penicillamine — B, B - dimethylcysteine. Ca DTPA — Calcium salt of Diethylenetriaminepentacetic acid. CDTA — Cyclohexane 1, 2 - transdiaminotetraacetic acid.

Penicillamine has been tried in handling abnormal copper metabolism for Wilson's disease. Diethylaminetriamine pentacetic acid. This surely suggests that the concept of complexing damaging metals has caught on and will be developed with safe, manageable compounds in the future to take care of the damaging effects of metals.

DR. H. N. SANFORD: It is unnecessary for me to say that these papers have been excellent. I do feel, however, that there were some things mentioned that should be thoroughly emphasized, principally that we do have a very serious problem of lead poisoning in children which is based on certain factors.

First is the age of the children, usually 18 to 36 months, because that is when they begin to walk around and pick up things. Second, they must have a certain environment, a home where the inside paint and putty is over 50 years old, so they can obtain the lead from the old paint that flakes off. And finally, this usually occurs in hot weather, when dilated capillaries and a mild acidosis bring the absorbed lead back from the bones into the blood stream.

Here in Chicago, for example, we only observe the severe symptoms of lead poisoning from June to September. They occur in every hot spell. All of the children we see during the year with lead poisoning are during those months.

The next important point is that of diagnosis, which is rather simple. As a history we have the factors I have mentioned. Clinically we have a child who is irritable, has anorexia, is losing or not gaining weight, has persistent constipation and periodic vomiting with no particular reason or discomfort.

We have the rule in our clinics that if such symptoms occur in a child of this age group in the summer time particularly, or even at any other time, these children must have their urines examined for coproporphyrins. I did not hear this mentioned, but we have found it to be a most reliable screening test and very simple to do. All you need is 5 mls of urine, 5 mls of ether, three drops of acetic acid, and shake well. This is examined under a Wood's light after 15 minutes. If the child has an excess of lead excretion, the urine will show a reddish color. Intensity of color is not consistent with amount of lead excreted. If you get any reddish color change at all, the child has lead poisoning.

The next important thing is to initiate immediate treatment. Don't delay. Obviously the child should be removed from the source of lead, but this is of course not always possible. Next, active attempts should be made to get the lead out of the tissues. This can be done by a variety of methods. Twenty-five years ago we used to alkalyze the child; however, we found it was more dangerous to pull the lead out rapidly than it was to leave it in.

I agree with all the therapeutic measures mentioned, but I would like to emphasize that initially the edema is more important than the encephalitis. Last year I got to the point where I felt that a decompression should be done on all of these children as soon as they showed the slightest signs of encephalopathy. This year I have changed my mind somewhat because we have had good success with the immediate use of certain dehydrating agents such as injectable urea (1.5 gm per cc). So far this year we have used this initially and have not found decompression necessary. The main point is to do one or the other at once and not wait for increased pressure and convulsions.

DR. R. S. BYERS: Lead poisoning in children still does occur in the winter. We had one last January or so who died of lead encephalitis, following chicken pox, which, of course, doesn't respond to any of the drug treatments. He started to vomit and became unconscious. This was erroneously ascribed to chicken pox encephalitis. Nobody looked for lead because it was January. Remember, it does happen.

We have the same seasonal peak in Boston, exacerbation in the summer months, but still there are cases at other times of the year. There must be other factors than heat or sunlight or vitamin D that precipitate lead poisoning in some children and in other periods.

We had a bad accident with oral Versene when it was first under investigation. Our practice was to take the children in, get 48 hour urine sample to substantiate the lead poisoning, clean out the GI tract and give them some oral Versene. By mistake one child got oral Versene on the first day in the hospital. The child fell unconscious. He had not been seriously ill before, but his lead excretion went to something like 18.5 mg in the next 24 hours. His spinal fluid, total protein, went up very markedly from somewhere around eighty to somewhere around 400 mg %, and I am sure that he was badly injured by this experience. If you give oral Versene with lead in the GI tract, you not only absorb the Versene but also absorb a lot of lead along with it. The Versene-lead combination isn't a one-way street, and it is possible to break it down in the tissues, and give out lead.

Then the last point I would like to make is about porphyrin excretion. There is a little evidence that sunlight has something to do with increasing the porphyrin output in existing lead poisoning. De Mole, I think it is, has inoculated rabbits and other animals with lead and exposed them to ultraviolet light with other things remaining constant and gotten a great increase in the amount of porphyrin output in the urine of these animals, so that sunlight, as other people have suggested, not only has something to do with the absorption of lead, but also has some effect on the metabolism of lead after it is in the body.

DR. H. H. STEINBERG: Before we get too enthusiastic about EDTA, I should like to caution you against considering it as a panacea in the treatment of lead poisoning. I believe it may have a real place in the treatment of acute plumbism in children.

I should like to caution you against its use in adults since many cases definitely diagnosed as industrial lead poisoning get well without the use of EDTA, and almost without the use of any definitive treatment. As was so clearly shown by Kehoe so many years ago, by removing these people out of the lead environment and treating the colic or anemia, these people get better.

The use of EDTA will never eradicate lead poisoning. As a matter of fact, Dr. Johnstone a few years ago in St. Louis pointed out that one of the plants in Los Angeles had stocked its shelves with EDTA instead of inaugurating a control program for the reduction of atmospheric levels of lead in the environment to safe levels. I think the important problem is, as Drs. Hardy and Remlinger emphasized yesterday, the one of diagnosis.

We are not educating the house officers, residents and hospital interns. We are not getting to the general practitioners nor the industrial physicians who must diagnose and treat cases.

I would suggest that organizations such as this one, universities, industrial medical groups or medical societies establish panels of qualified physicians in the occupational diseases, so that doctors or house officers can consult with these physicians for advice as to diagnosis and treatment.

CHAIRMAN WHEATLEY: The next paper: "Progress Report on an Experimental Investigation of Factors which Influence the Responses of Human Subjects to Finely Divided Lead Compounds in the Atmosphere," by Dr. Robert A. Kehoe, Director, Kettering Laboratory, University of Cincinnati College of Medicine.

PROGRESS REPORT ON AN EXPERIMENTAL INVESTIGATION OF FACTORS WHICH INFLUENCE THE RESPONSES OF HUMAN SUBJECTS TO FINELY DIVIDED LEAD COMPOUNDS IN THE ATMOSPHERE

By ROBERT A. KEHOE, M.D.

I have made use of an unsatisfactory title for my contribution to this program because I didn't know how to give a better one. Perhaps you may come to the conclusion that it would have been better had we gone on with the discussion of the subject that we were dealing with just prior to this time.

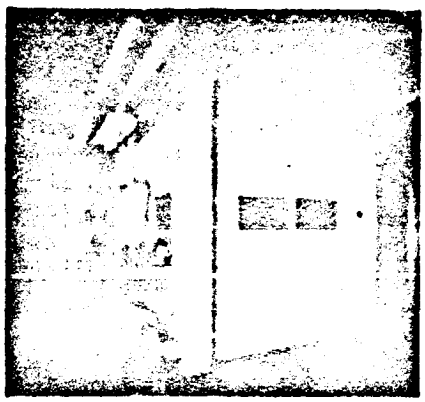
I want to explain my purpose, however, and call your attention to one or two things which I think are of fundamental importance. We shall understand the problem of lead poisoning better when we understand the metabolism of lead in the human organism and when we know more about the physiology of this material, of this mineral element.

It may be of some interest to recognize that we probably know more at the present time in the field of the mineral metabolism about lead than we do about any other element. I see a shaking of heads. This is only because there are some new elements which, because of their newness, have been looked at with considerable intensity. But with respect to the older elements, those that we have been concerned with for the long pull — those which, because of our familiarity with them, we tend to think of as being well understood — I think I can say with reasonable safety that we probably know more about this in relation to lead than we do in connection with any other metal.

In any case, I wish to recount to you, in a very short space of time, what we have been undertaking to do over a period that began in 1965 and is still continuing: to further elucidate the metabolism of lead in the human organisms. After this, if time permits, I shall wish to refer to some practical considerations that relate to diagnosis and to industrial hygiene.

Over this period of time in the Kettering Laboratory, we have been devoting ourselves to a basic study of this problem. It began with an attempt to elucidate the occurrence and the distribution of lead in nature and in biologic materials. This has not been by any means completed, but the essential contributions which we have made to this field were published in their initial form in 1933. Then, a few years later, we began to study the metabolism of lead in human subjects under conditions of both normal and abnormal intake following the oral administration of lead, undertaking to determine precisely what happened under the conditions of prolonged, continued administration at variable levels of dosage.

The results of these investigations have not all been published, but to the extent that they have been published, they appeared over a period of several years, ending about seven or eight years ago. Then about eight years ago, we began to study the other important variant of this problem, from the point of view of industry, namely — what happens to lead which is in the respired air; how and to what extent it is respired and retained in the pulmonary apparatus, what happens to the rates of absorption, retention, excretion under these conditions.



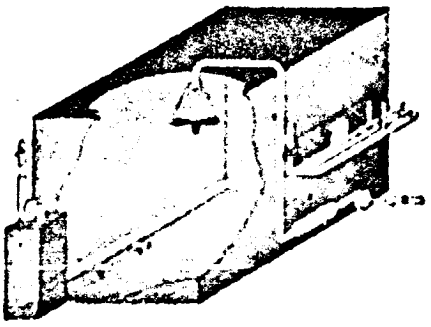


Figure 1 (Left)
Figure 2 (Above)

now six experiments on four subjects, two of which have been duplicated. We are able to report our progress, and my reason for reporting this verbally is that it is, I think, unsatisfactory to publish this material in titles here and there, in bits and pieces. Such reporting fails to accomplish our purpose, in that, as we have seen here today in the questions that have been raised, the pertinent facts about which we are in doubt cannot be presented fully and systematically.

In short, serial brief publications fail to present the problem in all of its facets in such a way that one can grasp its full significance. Therefore, we have withheld publication, and this is the third verbal report that I have made to interested groups as to what we have learned up to the present time.

I would like to discuss the backgrounds of this work further, but I may say that its primary objective is to understand the problem and all of its ramifications as far as we can under the controlled conditions of laboratory observations on human subjects. If a more specific objective were in mind in the group of experiments that are under way at the present time, it is the idea of appraising the whole area of respiratory exposure to lead in terms of such things as the standards that we are concerned with in the field of occupation; the standards which relate to the exposure to lead on the part of the community in general, with respect to what is safe on the background of our knowledge of the normal metabolism of lead; of the unavoidable exposure to lead, plus what we have learned in addition from industrial experience.

Beginning with Figure 1, we have a respiratory chamber, the outside of which is illustrated. Essentially this is a chamber made by the use of standard metal partitions that are available at the present time on the market, plus the introduction into it of the necessary ventilatory and other equipment that would produce a dynamic experiment by which we can introduce into the atmosphere of the chamber a known concentration of a known compound of lead in a known state of subdivision, in which an experimental subject carries out his day's work on five days of each week for seven hours and a half a day. This procedure simulates the conditions of industry, but not those of community exposure to lead in the atmosphere.

Figure 2 merely shows some of the details: the intake of air, the course of distribution of the stream into the chamber, the use of a fan below and at the end of the influent tube to dissipate the air throughout the room instead of using a mechanical distributor which would in-

the bottom is the means of removal. The material passes through an electrostatic precipitator to the outside where it goes into one of the main stacks of the laboratory, and the experiment is, therefore, contained within the unit area of the chamber itself.

The equipment located outside the chamber on a shelf is the means, in a specific experiment, of introducing the lead compound into the chamber at a known rate and concentration.

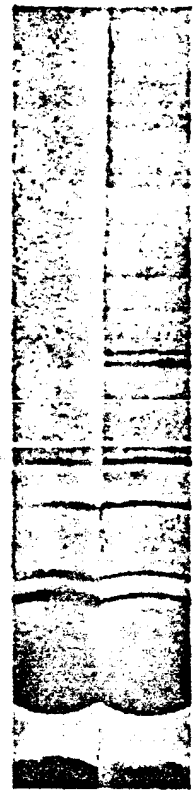


Figure 2

This room is equipped as an office. One cannot use an experimental subject in this kind of experiment without giving him something to do other than twiddling his thumbs for five days a week, seven and a half hours a day over a period of months, weeks or years.

The methodology from here on is that of having the individual who is the experimental subject collect precise duplicate samples of everything he eats and drinks in the course of a day, to collect all urine voided, to collect all feces passed in the course of this period of time and to maintain this regimen daily throughout the period of the observations, including a period of not less than six months preceding his introduction into the chamber, in order to establish the pattern and the character of his lead metabolism.

I might point out to you at this point that while it is necessary to establish the initial metabolic pattern of this individual, this procedure does something more. The pattern of the lead metabolism is so clearly established in terms of present day community life that we can very easily detect not only whether a subject is normal in his behavior, but also whether or not he is a reliable subject. If he deviates much from

which in this instance demonstrates the nature of the compound used. Since our early and traditional experience in this area of lead in the atmosphere has related lead oxide, we have chosen, for historical reasons and also for the ease of doing it, to use lead sesquioxide which is produced by the combustion of a small quantity of tetraethyl lead in a stream of propane through a Bunsen burner. By this means, you can regulate the size of the particle and the concentration of material entering in terms of the speed at which the tetraethyl lead is fed to the propane stream.

This provides a completely reproducible system for producing lead of a known size of particle, of a known chemical character, and at a known and very steady rate of production.

Figure 4 shows the electron microscopic picture of the lead compound used in the chamber, in this particular instance, in an experiment in which lead sesquioxide of the mean size is .05 micron. (Individual particles in small numbers are as large as .17 micron.)

Figure 5 shows the distribution of the particle sizes, and you may see that there is an even distribution of the particles in the chamber.

Figure 6 illustrates a troublesome procedure and one I may say that is still troublesome. This method shown is not entirely satisfactory. We are put to the necessity, in determining how much lead this individual takes in and retains under these conditions, of being able to determine the lead in the expired air, and we have devised a simple method of doing this. It enables the individual, while breathing air contaminated with lead, to expire through an electrostatic precipitator into a Douglas bag. The expired air passes through the precipitator first at the shortest possible route, rather than through the Douglas bag. By this means we have been enabled to determine approximately, at least, the extent of the pulmonary retention of lead, and you will recognize that on the basis of the calculation of the lead concentration in the air and knowing the respiratory volume and rate, we are able to determine what portion of the lead breathed in in the course of this seven and a half hour period was actually retained and absorbed, and we are able to determine, as I will show you later, something of what its fate has been.

As I indicated, we have done six experiments, one of which continued for five years and two months. The second one continued for four years and four months; the third one for two years and six months; the fourth one for two years and seven months; the fifth, for two years, and

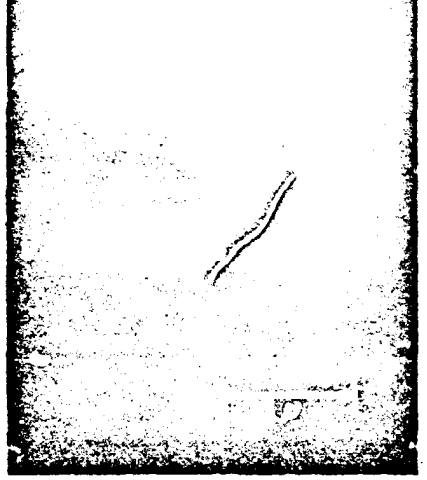


Figure 4

the one which is at present in progress has now gone on for a year and a half and will not be completed for another two years.

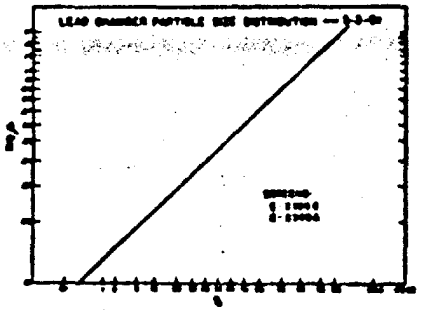


Figure 5

These are troublesome experiments to carry out, costly in terms of the time and effort of all

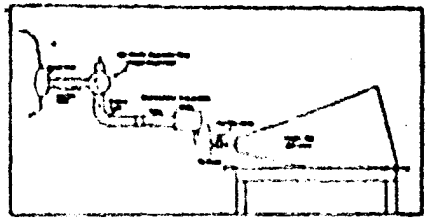


Figure 6

been raised here this morning and through yesterday about the oddities of the behavior of lead under a variety of conditions can be answered satisfactorily in no other way than by this method.

Since time will not permit me to go into the individual experiments, let me conclude with these few remarks.

There have emerged from these experiments thus far, in accordance with the variables of dosage and particle size, three major facts. One of them is the discovery of what happens when the respiratory exposure is discontinuous. The individual reaches a plateau, with respect to his rate of urinary excretion and the concentration of lead in his blood, when he is exposed for five days a week rather than seven. If we give lead by mouth every day, or seven days of each week, the concentration in the urine and the accumulation in the body goes up at a steady, essentially constant rate throughout the whole period of exposure, for as long as five years.

In these experiments the subject reaches a plateau in from six to eight months, at which time the height of the plateau is indicative of the severity of the conditions of the exposure.

The next point, and the one which I wish to emphasize at this time, is that when we change the size of particle two things

35% to 40%. With a larger particle of about one micron we note a slightly greater pulmonary retention, around 40%, 45%, up to 50%. A very considerable proportion of the particles of 3 microns is strained out in the upper respiratory tract and appears in the feces. At this point the level of the fecal content is differentiated sharply from that due to the food and, at the same time, the total rate of lead absorption, in proportion to the lead content of the air, decreases.

I think you will understand why I said, at the start, that it would be difficult to present to you much in the way of an account of what has been done and learned by these experiments. I have believed it to be worthwhile, however, to bring you a progress report indicating that this work is continuing, and that we are carefully examining step-wise the factors that influence inhalation, as well as those which influence absorption and excretion under the conditions of inhalation.

MR. MANFRED BOWDITCH: Our Chairman, Dr. Wheatley, has been obliged to leave. He had to be at a meeting in Washington later today.

It is quite obvious that we are going to continue here after lunch, and if Dr. Lauer doesn't mind, I am going to ask him to postpone his discussion of Dr. Kehoe's paper until we meet again after lunch.

FRIDAY LUNCHEON SESSION

November 7, 1958

A SUMMATION OF THE CONFERENCE PROCEEDINGS

By THOMAS L. SHIPMAN, M.D.

CHAIRMAN MAJ. FRED BOWDITCH: The summation will be given by our old and good friend, Tom Shipman, Health Division Leader of the Los Alamos Scientific Laboratory, Los Alamos, New Mexico.

DR. THOMAS L. SHIPMAN: This has really been one of the most stimulating and enjoyable meetings that any of us, I think, have attended. There are few industries that are as ready and willing to air and discuss their problems as the lead industry. I am sure that every one of us feels that the Association is to be congratulated and thanked for providing this opportunity again to consider the problems of lead. And, Mr. Wormser, I hope that you will transmit my feeling on this to the other officers of the Association.

MR. F. E. WORMSER: I will be glad to. Thank you.

DR. SHIPMAN: Of course, it goes without saying that this engine has a sparkplug, and we know who that sparkplug is. The completely tireless energy of Manfred Bowditch is probably the thing which is largely responsible for the great success of this meeting, and again I might mention his subtle approach to those who are requested to speak, starting back early in the winter.

I would also like to express just a word of thanks and appreciation to the management of the Drake Hotel, which has made us all so comfortable while we have been here.

I have learned a lot in the last two days, and it is valuable knowledge. One thing that this session has emphasized widely is that in this whole matter of industrial health we are dealing with two skills, medicine and engineering. I do not think that either one is more important than the other, but on the other hand I would say this: The doctor by himself can do a pretty good job. The engineer by himself can do a pretty good job. But only by working together and appreciating each other's responsibility and point of view can they do the sort of rounded-out job that the enlightened demand.

Now to those of you with long memories, these words may have a familiar ring. They were spoken on this same occasion ten years ago by Dr. Lanza at the opening of his summary of the meeting. To the two skills, medicine and engineering which Dr. Lanza mentioned, I think we must add a third. As was so obvious this morning, the field of research is a bona fide member of the team. Today, I feel we must recognize it as such, recognize it cheerfully, and realize that research has much to offer, that bit by bit it is slowly unlocking the problems of the physiology of lead which have been puzzling men for over the past two thousand years.

The individual who is chosen to summarize a meeting of this sort is in a rather unenviable position. As a matter of fact, if there is anyone here who would like to take over this job, I would gladly change places with him. The question arises as to why Manfred selected me. I don't think that I have seen a case of lead poisoning since I was in medical school. We certainly have no lead intoxication at Los Alamos, although considerable amounts of lead are used in a variety of ways, and there is an extremely energetic industrial hygiene program to control it. Perhaps, however, having no axe to grind and coming at the problems from a relatively unbiased point of view, I can carry out a summary which may pull a few loose threads together.

I would like to mention each of the round dozen presentations that have been made, but I can only try to touch on them in groups.

The summariser is in a dilemma to know whether he should touch on only a few main points which have arisen during the meeting, or whether he should, piece by piece, go over and attempt to touch on every point. A second dilemma exists in that the summariser can only bring out those points which are of interest to him personally, and I am sure that almost any of you would give the summary in a very different way.

We started off yesterday morning with Dr. Belknap's paper, and immediately one quite important point emerged. This was brought out not only by Dr. Belknap, but also by Mr. Fallon, Dr. Reznikoff and Dr. Kehoe, all of whom stressed the danger of establishing a diagnosis of plumbism purely on the basis of laboratory tests. An individual with plumbism is a sick person. The diagnosis must be established by the acumen of the physician on the basis of history and physical examination, and with the confirmation of laboratory tests of a wide variety.

In considering the various papers which have been given in the past two days, it is rather interesting to go back to the proceedings of the meeting ten years ago and find that most of the papers given today and yesterday have counterparts in papers given ten years ago. Dr. Belknap's paper had two counterparts, the papers by Lanahan and by Silsen.

Mr. Frank's paper on "Health Control in the Ceramic Industry" had a counterpart in the paper given ten years ago by Sherman Pinto. Mr. Frank's paper expressed, from the point of view of the safety engineer, and Dr. Pinto's from that of the physician, the necessity of pooling the various skills — the physician's, the safety engineer's and the industrial hygienist's — in a control program in industries using lead.

Dr. Schrenk brought out some points worth remembering. In his paper he brought up the fact that the numbers used for maximum allowable concentrations, of necessity must be used as guides, that they are a compromise, representing the pooled knowledge of a group of experts.

They represent a compromise in another way, too. I think all of us will agree that the only ideal dose of any toxic material is zero. Establishing a maximum allowable concentration, therefore, must be a compromise between zero and an obviously toxic dose. This is clearly true in the case of radiation, the field with which I am the most familiar. We would like to have zero doses to radiation as we would like to have zero doses to lead throughout industry.

One other point should be kept in mind. Mention was made of the occasional lowering of maximum allowable concentrations or permissible doses. In some cases it is perfectly true that a lowering of a maximum allowable concentration represents new knowledge, that the material is in truth more toxic than it was thought to be. In some cases, however, a lowering of this sort may reflect only an improvement in our own terminology and our ability to protect people, permitting us to approach more closely the zero ideal that we should strive for.

It certainly is to be hoped that the controversy of lead paint inside tanks now has been ended. Indeed, the discussions of Hervey Elkins and Herb Stokinger on this subject were thoroughly convincing to me, and I certainly have no worries about drinking water that came out of a tank painted on the inside with lead paint.

I would like to mention one point that arose in my mind while listening to Ichirman Byers. Our methods for analysing blood, urine and air for lead are constantly improving, although they still leave something to be desired. One thing which we have not yet been able to do is to study, not the amount of lead which is being excreted, not the amount of lead which is circulating in the blood, but the amount of lead which is fixed in bone where we can't get at it; it seems to me that it is as important to know what is left behind as it is to know what has been excreted.

We really don't know accurately what the body burden — the total burden of lead in a case of plumbism at any degree you choose to mention — is.

As we were coming over here in the plane, the day before yesterday, Dr. Foreman pointed out to me a phrase in a paper by Lockie and Tompsett from the *Quarterly Journal of Medicine*, January 1958, which I would like to read: "In any group of people exposed to the hazards of lead absorption a limited number of cases of frank poisoning will result. In the remainder, however, signs of toxicity will not appear, the skeleton having successfully immobilised the major part of the absorbed lead.

"There is good evidence to suggest that many forms of acute stress" — and here he refers to work of Aub, Fairhall, Minot, Reznikoff, Brown — "can bring about release of this skeletal lead and give rise to symptoms of lead poisoning."

I think this is something which we should keep in mind. In the case which Dr. Hine quoted yesterday, and which has been referred to by Harriet Hardy and others, the reappearance of circulating lead, the release of circulating lead, is a matter of interest.

This meeting, of course, would not have been complete without John Fouiger. As I sat listening to him yesterday, an image came before me. It was at the time of the Spanish Inquisition and John was one of the judges, and I just thought how I would hate to be the poor heretic that was brought in front of him. [Laughter]

The statements which he made, I think are incontestable. He is opposed to sin and in favor of virtue, but he has given us some very good definitions of what sin and virtue are.

I will just point out one thing that he said: a compliance with statutes does not provide immunity; good faith is required. That, I hope, will be remembered.

Ten years ago there was a paper given by Dr. Johns. This year we added *four* to it, and there was a very similar paper by Red Johnstone. Ten years ago Dr. Lanza pointed to the fact that Dr. Johns visited his patients. Dr. Johnstone brought out the fact that he visits them, understands them, talks to them. All of you here, I am sure, are aware of the languages that arise in different industries and of the inability of the average physician to know what these people are talking about, to get any kind of a visual picture of what their occupation really consists of.

My introduction to industrial medicine a good many years ago came from a dear old gentleman whom a few of you may remember, Dr. Frank Schubmehl, at the General Electric in Lynn. Dr. Schubmehl told me once how he evaluated a doctor in industry. He would visit a plant and have the doctor take him around through the shops. And if, universally, the workmen turned from their jobs and said, "Hi, Doc," he felt that that doctor was probably all right. An intimacy between industrial physician and workman is the *sine qua non* for the establishment of the confidence which obviously must exist.

As for Ted Waters' paper, he dwelt on worries that have bothered him. I don't think there is anyone who is better qualified to consider the legal problems having to do with industrial medicine than Ted, and certainly if we lump together the statements made by John Fewiger, Ted Waters and Arthur Johnson, we have some things to remember.

In Arthur Johnson's paper, I particularly remember his statement about the three criteria for acceptance of liability in compensation cases. First, the establishment of a true and positive diagnosis. Second, the establishment of an actual causative factor for the disease in question. Finally, the existence of true disability. I only wish that all of the members of all industrial accident boards understood this as well as Mr. Johnson.

Ten years ago there were two areas which really presented something new, something which probably would not have been considered had there been a meeting before that, in 1938. One of these was the study of solubility and particle size, an area which was not strictly new to some investigators, but I think it was rather new to much of the group at that meeting. The second new topic was the use of BAL in the treatment of plumbism.

Again this year we had two things that were new. We had Anne Baetjer's work on the effects of temperature, humidity and seasons, and the two papers on the use of EDTA in treatment. Anne Baetjer's paper, in my opinion, was outstanding. It has been a difficult job, and I feel that the work which Anne presented this morning is to be regarded as only a preliminary report. Obviously much remains to be done, and I can visualize her next headache of trying to reproduce this whole thing with immature, growing mice, not adult mice.

Now, EDTA was not mentioned ten years ago. It didn't exist. BAL was the new thing, but in his paper on BAL Dr. Eagle said: "I wish to suggest that although BAL has proved so effective in the treatment of certain types of heavy metal poisoning, there is no reason to believe that other compounds may not be developed which are even more effective and which, acting on the same principle as BAL, may serve to abstract lead from its combination with tissues."

I feel very certain that at the next session of this meeting, ten years from now, EDTA will have passed into limbo, that we will have new compounds which will do the job very much better than BAL.

We wound up with Bob Kehoe's paper, and it was impressive. What they are doing at Kettering is research in the grand manner. When you stop to consider the dollars, the man hours and the boredom [Laughter] that has gone into this — I don't want to sit in one of those chambers for seven and a half hours a day even if you give me a desk and a radio! [Laughter] But this is really the fundamental approach. This is using men, getting him in what most nearly approximates a toxic working environment and studying him. It is a tremendous chore, and I believe that Bob and his associates at Kettering are to be not only congratulated but encouraged to keep it up.

I am sure that I do not have the last word here, because all those who still wish to talk will have ample opportunity this afternoon to get questions or answers off their chests. We have had, as I said, a splendid meeting, and it is with great pleasure that I now turn it back to Mr. Bowditch.

CHAIRMAN BOWDITCH: We will reconvene at ten minutes of two, starting off with Dr. Lauer's discussion of Dr. Kehoe's paper, for which there wasn't time this morning, and we can then continue with whatever of the various subjects of the past two days anyone desires to discuss further.

FRIDAY AFTERNOON SESSION

November 7, 1958

Discussion of DR. KEHOE'S Paper

and

ROUND TABLE DISCUSSION

CHAIRMAN MANFRED BOWITCH: We will proceed with Dr. Lauer's discussion of Dr. Kehoe's paper.

DR. JOHN LAUER: I was certainly impressed with the tremendous magnitude of the research study undertaken by Dr. Kehoe and his group. Eight years ago, I had the pleasure and privilege of being among those who participated in the start of this study. In the past seven years, I have had little or no opportunity to follow its proceedings. It seems that a work so extensive and important, delving into the metabolic relationships of lead, could hardly be done justice in twenty minutes. By the time Dr. Kehoe had had the opportunity to sketch a little of the background of the experiment, there was little time left to permit us to digest what was found.

From the charts that were put before us this morning a few questions arose in my mind. One is, following the period of the inhalation of lead sesquioxide, there was a rise in the blood level and, concomitantly, in the urinary excretion of lead. If I noted correctly from the charts, the excretion dropped off in the urine rather abruptly, whereas the content of lead in the blood, after discontinuation of exposure, tapered off rather gradually. If I remember correctly, in your early work in the Twenties and Thirties, when lead was given by mouth, after the dosage period was over the excretion tapered off over a rather long and gradual period. This did not seem to be true in the subjects shown here this morning. I would ask for comment on that.

Another point that wasn't clear to me was the matter of some 30%, or 40% of particles which were retained in the respiratory tract following additional exposure. I wonder if this was retained, or deposited on the respiratory mucosa. If it was deposited, how much of it was lost in the mucous and therefore swallowed later, or expectorated?

I think all of us are looking forward to the final publication of this work. It is of such magnitude that one must sit down and actually study it before reasonable comment may be made. I now invite discussion of this paper.

DR. D. P. LAUGHNOUR: This work of Dr. Kehoe's ties in completely with what we must know in order to know about what we are going to accomplish, or are accomplishing, with the use of EDTA. There have been numerous reports of cases that were treated by EDTA which indicated that at the end of a relatively short course of treatment, the urine and blood samples had returned down to what we consider a normal level. Long-continued exposure, as we have in many cases of industrial lead poisoning, also indicated by Dr. Kehoe's work, shows that these cases, if left alone to the normal metabolic and excretion processes, would take approximately twice as long to return back to the normal line as they were in getting up to their high level.

Someone else commented to the effect that EDTA, in forming a chelate with lead, was not a one-way proposition, but followed the laws of chemical balance, in that there is always a reversible action and it simply goes in one direction to a point of chemical balance.

If this is so, then it would be possible, in giving EDTA in too large a dose, to increase the actual toxic amounts of ionizable lead present in a critical case of toxicity, such as in a child with encephalitis. In my experience with results and data in the use of EDTA, I have had no case that has returned to normal levels, even after prolonged use of EDTA far past that required for the relief of symptoms. Although urine levels would return to non-exposure levels after six to 12 weeks' freedom from use of the drug, they still came back to practically the pretreatment levels until after three to six months' intermittent use of EDTA. This is exactly what one would expect from Dr. Kehoe's presentation, unless the drug were continued over a period of time that would be roughly proportional to the time that this patient was absorbing his lead, acted upon by the factor of the increased excretion due to EDTA. In other words, if a single injection of EDTA caused a 30-fold, 24-hour excretion of lead, we would have to say that that represented 30 days instead of one day of getting rid of the lead; and, of course, as the EDTA continues to be given,

the amount of lead excreted falls until it reaches a level where the mobilizable lead outside of the bones is all excreted. But as soon as time allows, chemical equilibrium brings the blood back up to the balance — determined by the total amount of lead in the system, which means in the bones. Therefore, to accomplish deleading, EDTA would have to be used over a period of time twice as long as the patient was accumulating his lead, divided by the multiple of the number of the rate of excretion caused by EDTA, and in most cases EDTA has not been used that long.

DR. ELTON L. SELKNAP: Yesterday, Dr. Reznikoff emphasized the importance of the clinician considering all the diagnostic possibilities in a lead exposure case, including non-lead conditions. I have two cases in point in the hospital right now. They were operated upon within the last week. They both presented themselves as "foot-drop" due to lead. They were fortunately not from our plant. In fact, we have never had a case of foot-drop in our own storage battery industry.

The places where we see most of the peripheral neuritis lead palsy cases — there are not very many of them, I have probably seen only six or eight — have been in the brass foundries where there is a long-continued low exposure, with a low level of lead absorption.

One of these cases was a furnace charger in a smelter which was melting up old smashed battery plates. Though it was a relatively small operation, they usually were able to melt up two or three of these big semitrailer loads of smashed batteries.

They had only eight or ten men exposed. This exposure was so intense at first, however, that at one time I recommended that the plant be closed, pending adequate engineering ventilation. Thereafter, the cases were not sent to me.

They are still in operation, with only a fair amount of engineering control. One of these men I had first seen in 1951 or 1952, when he was charging a smelter from a small scaffold, with the fumes so intense that when I was up there standing next to him, I couldn't see him because of the fumes that were blowing back out of the furnace. Inside of two or three minutes, I was tasting plenty of sweet lead. He still had been working there, and he finally developed a foot-drop. He had drifted around from one hospital to another. They first thought he had congenital porphyria. When he was finally sent to me for evaluation, I believed that he had a mild foot-drop, most likely on the basis of the lead absorption. But there were certain aspects of the case that did not seem clear and that didn't add up to show that lead was causing all his symptoms.

He was having increasing paresthesia, or numbness, and crawling sensations of his lower legs, extending up toward the chest, with a constriction distress from the epigastrium right through to his mid-back. None of that sounded like lead to me. However, we did treat him for the foot-drop with Versene intravenously. With the resultant increase in lead excretion, the foot-drop disappeared entirely. However, he still had these other symptoms of paresthesia, so we had a myelogram done on him because I didn't want to turn him out. The lead liability was over with the clearing of the foot-drop. A myelogram was then done, and we found a space-occupying lesion from the fourth to the sixth dorsal vertebra. A neurosurgeon operated on him this week and found a localized arachnoiditis. The patient had had treated lues in the past. This was so localized that it was beginning to pinch off the spinal cord itself.

That is one case where, if we had not pushed the diagnostic procedures more or less to the nth degree, probably somebody would have made a claim that this entire situation was due to his previous lead absorption. The operation showed really a localized spinal cord lesion unrelated to the occupation.

At the same time I have in the hospital another man with a bilateral foot-drop. The attending neurologist felt that it must be due to lead. This man was a hunter and told me at great length how he never even bothered to sift the lead shot out of the duck that he killed and ate, but just swallowed it, lead shot and all. He was also operating a small stone-cutting operation, where he used a lead-containing lubricant on his machines. Whether that had anything to do with it was questionable, but anyway, he did have a border-line blood and urine lead, but no stippled cells and no lead line. He certainly had a foot-drop, but then he began to develop weakness in his hands, in the extensors.

I myself have never seen a quadriplegia due to lead, but he had been rapidly developing that in the last few weeks. We also did a myelogram on him. We found that he had cervical and lumbar discs. Later, the cervical disc will be removed, with probable cure of the quadriplegia.

There was another case where there was lead in the background. If we had not followed it through because it appeared atypical for lead, I am sure that the insurance carriers in both cases would have been paying permanent total disability before long.

Yesterday Dr Hardy spoke of plumbism as still being present in modern industry. I certainly would agree with that. It still seems to crop up in the most unexpected places, particularly in the small, unsupervised plants.

I would like to quote briefly two or three

out that he was baling paper which contained lead arsenate from a nearby insecticide plant. When he jumped up and down in the press, he stirred up plenty of lead dust, with resultant inhalation.

Soon this patient wandered into a hospital. Nobody knew what was the matter, he was so confused. However, when the technician in the hospital found 400 stippled cells per 50 fields, she told the residents they had better look at the patient's gums. They then found that he had a lead line from ear to ear.

Another such case of unsuspected lead absorption was from an eight-man brass foundry where the boss himself was the first man to get lead poisoning. He had many stippled cells and a lead line. There were five cases of lead intoxication — lead colic type — in that eight-man brass foundry. They had just started to pour brass, though they had formerly poured aluminum. They knew nothing about the fact that there was lead in brass.

Another small shop of eight or ten people was making an "oilfree" lubricant. You may not have heard of that. They bore holes in bronze bearings and fill the holes with so-called "marvelous oilfree lubricant," incorporated in a wax stick. Investigation finally showed that the lubricant contained 90% lead oxide. I happened to see this case after the man had died. Nobody had any idea, even the boss, that there was lead in that lubricant. The patient would put this on a lathe and smooth it down with a file, blowing the lead lubricant dust directly into his face. The man was scheduled to have an operation for brain tumor, before a blood count revealed many stippled cells and close study also showed a marked lead line on the gums. The man died a few hours after the operation, and then the occupational exposure was suspected. Then I was asked to investigate.

Now, all of these last three cases had lead lines and stippled cells. I think this underscores the importance of considering the commonest type of lead diagnosis, using the simple methods of study for lead line and stippled cells. Lead poisoning, much of it unsuspected, is certainly still with us.

To conclude this summary, I believe that after a careful consideration of history, including occupational history and a plant tour by the doctor, together with physical examination, looking particularly for a lead line and stippled cells, and ever quantitative lead studies of blood and urine, I still would make an urgent plea not to throw any very useful diagnostic tool out of the window. I refer especially to

I know that such study has recently been called an antique method, but whatever method is used, whether you use stippled cells or quantitative lead in urine or blood, I think there are two important things to be considered. First, these studies should be done serially and frequently; and second, the physician himself should study the actual work exposure of the lead worker.

CHAIRMAN BOWDITCH: Are there any comments on other papers?

MR. ARTHUR JOHNSON: With respect to labeling laws, a point that everybody knows perfectly well, but it has not been expressed at this meeting, and it might just as well be tucked into the record — much has been made of the fact that you can understand and believe the law, and comply with the law. That is what Dr. Foulger said; but you have to demonstrate good faith, all of which we understand and agree to.

The fact remains that none, or all, of those three things accomplished, will let you off. The best that labeling does for you is to provide some evidence that is admissible in the trial of your case, and the jury will decide how much weight they want to give it.

Just a point that it is not prima facie evidence that you have absolved yourself from all liability. You merely have some defense that you can present as evidence, and the judge has to put it before the jury as good evidence.

I have two additional comments on the labeling of paint. Childhood plumbism is found almost exclusively in slum areas where lead-containing paints have fallen into a deteriorated state. Poisoning rarely occurs where surfaces are maintained in a good state of repair. Labeling of paints will help "do-it-yourself" parents and home-owners to select safe paints for indoor surfaces, children's toys and furniture. Labeling will not solve the problem of deterioration. If communities wish to reduce their incidence of childhood plumbism, they must acknowledge and implement the need for maintaining houses in a good state of repair.

CHAIRMAN BOWDITCH: Is there any further discussion of this interesting subject? If not, we come now to Dr. Johnstone's "Common Errors in the Diagnosis of Plumbism."

DR. RUTHERFORD T. JOHNSTONE: I am not going to comment on my paper. There was enough. But I would like to ask a question which shows my profound ignorance in this thing.

In industry, as you know, encephalitis from ingestion of lead is no problem. I want someone in this audience to explain to me why children get encephalitis by ingestion.

Our trouble in industry, of course, has been by inhalation. We have the reversible things, you understand. The second question I would like to ask is, in what kind of case is it felt necessary to use EDTA?

DR. J. J. CHISOLM, JR.: Dr. Johnstone, the excretion of lead in the feces of these children ranges as high as 100 mg of lead per day. This is five to 50 times the values reported for industrial types of exposure. The increased incidence of acute encephalopathy in children as compared with adults depends, at least in part, upon their more intense lead exposure.

DR. R. K. BYERS: I haven't measured nearly as many cases as Dr. Chisolm. It certainly is true in the few chips I have measured that I have seen children eat. It is quite obvious that the exposure is enormous. Whether the child's greater inefficiency of pH control and chemical homeostasis adds to the hazard, I don't know. I had a feeling it did. I think the exposure factor must be the most important one of all.

DR. M. B. SMITH: I, too, would favor the opinion that this is a dose factor primarily. We see that some of the levels of lead in the blood are very high as well. Chisolm has already described the stool findings, and such intense exposure is apparent in the slide I showed on the child that died.

I don't think that susceptibility is particularly a factor in terms of the central nervous system of children. We do see a collection of diseases involving the neurological system, where age probably is a factor because myelinization of the central nervous system hasn't occurred until the latter part of the first year; but myelinization is pretty well completed by the time the child gets to the age when lead poisoning occurs.

DR. HARRIET HARDY: I was wondering if Dr. Smith could tell us what amount of lead was in the brain tissue of that autopsy of the child, and other autopsied children. I am still interested in the idea that there is some difference between the adult and the child in what the central nervous system does in response to toxic insult.

DR. SMITH: No, I am embarrassed. I don't have it on that individual's slide and still haven't found the exact figure. I just have it from Dr. Kehoe. It was high in this individual child. In others, though, we have found that if there is less than .3 mg of lead per 100 gm of brain tissue, even though clinically someone has said there are indications of lead encephalopathy, Dr. Kehoe has been very hesitant to make this diagnosis; and on each occasion when he has been in the position of differing with those of us who were the clinicians, our pathologist has found another cause for death.

There have been several examples of this, and I think they point to the fact that even though there was a considerable amount of lead in the blood and in some of the other tissues, this was a coincidental finding in association with a disease which was itself fatal.

You asked this morning how our pathologist picked up this diagnosis. There were a couple of things that made him suspicious. In almost any case where there was evidence of acute cerebral edema and brain stem herniation, our pathologists have done two things: one, looked at the liver and kidney for the inclusion bodies that Blackman described a good many years back; and secondly, they have sent the brain, or parts of the brain, to the Kettering Laboratory for their confirmation by tissue analysis. The inclusion bodies are something that only make us suspect that this child has absorbed excessive amounts of lead. They don't prove the diagnosis of the encephalopathy. That requires the further step of cerebral tissue analysis for lead content.

DR. HARDY: In other words, this is a nonspecific cerebral edema having demonstrated exposure to lead by inclusion bodies or its presence in tissue. It then remains for someone to take the bold step and say they belong together.

I think it is perfectly possible that children with varying degrees of cerebral edema might have quite serious morbid change and physiologic change disturbance in intelligence quotient, or perhaps go blind if they lived. I am interested in what causes the patient to die, and whether it is related to lead in the brain of adults as well as in children.

I remember so well discussing the case of a Negro maintenance man in a storage battery plant who had had good, solid exposure and was found dead in his bed in his boarding house, and the case was brought up. Question mark — lead poisoning? There were staggering amounts of lead in the brain. In the discussion, I was the only one who was willing to put his death and the findings of lead in the brain together.

How much do you want to say that cerebral edema is lead-related? See what I am getting at? I am suggesting that the cause of death could have been heart failure, or excessive administration of fluids. But when does one say this is lead poisoning and lead-induced death? I am not saying it well, but I am trying to get at the problem of being so hesitant to say that lead is doing damage because you don't have as many pieces as you want in the equation.

I mustn't labor this point too much, but I see Dr. Byers wants to straighten me out.

DR. BYERS: I don't think I can.

DR. HARDY: I am just being difficult in asking the question.

DR. BYERS: Certainly when children die who have clinical pathological lead encephalopathy, they die with brain stem compression. They die with slowing respiration, pulse rate and blood pressure, anuria, all the usual evidences of increased cranial pressure.

I can't believe that this isn't in some way related to interference with the brain enzyme systems through amounts of lead which may not in themselves be impressive. We haven't as many analyses, I am sure, as Smith has, but again you find amounts of lead which are rather above the usual run in these children. We try very hard to find other causes for death. We certainly look for other diseases at autopsy and don't find them.

DR. HARDY: Could we bring it back to this original point of the difference between the adult and the child brain in its response to lead as a possible factor?

DR. BYERS: I think one factor that I can't tie in very well at this point of the argument, and which often is not appreciated, is the growth factor. I originally got interested in lead because of children who had had lead poisoning and had been sent home from the hospital as cured, who then turned up in my neurological clinic because they were misbehaving in one way or another, or not learning in school. One kid set the schoolroom on fire, another nice little girl danced around on the desk. None of these children had acute fulminating encephalitis. They all had evidence of lead poisoning, like stippled cells, some increase in spinal fluid, total protein, GI symptoms, coproporphyrin in the urine, things of that sort. At that time, we didn't know about the importance of separating them from lead. We tried, in a desultory way, to separate them. Maybe we weren't successful about that.

The point I am trying to make about these children is that though none of them, at two or three years, had an acute encephalopathy with their acute intoxication, when they reached six or seven they showed evidence of brain injury. I think that many children get chronic encephalopathy from lead, as well as this acute business. I think it is a question of degree where one merges into the other.

Now, with treatment with EDTA and with protection from lead, we don't see that picture as often as we used to. In fact, we haven't seen it at all in the last five or six years.

This group of children deteriorates gradually without ever having had any acute lead encephalitis, and therefore I think that lead does something to the growing brain which is different from what it does to the adult brain.

DR. HARDY: Now I have got what I want.

the effect of lead on the kidney.

I was excited by Dr. Chisolm's remark that they have been able to demonstrate renal tubular troubles and phosphate holding effects in children who have a lot of lead insult. I certainly have a small number, but a definite number, of men who have had long-term exposure to lead and who do show evidence of renal damage.

If you put that together with what Harry Foreman showed in experimental animals, what the Swiss have shown, and various other people, that if you give the right dose and give it rapidly, as Lasslo shows, you get damage in the kidneys — then EDTA must not be used in patients with evidence of renal disease.

I think another factor that leads to the decision to use EDTA in a practical way is whether the worker — the patient with lead poisoning — can forever after be free from lead exposure. If, for all the reasons all of us know, he may have to go back to lead, even under the best industrial hygiene circumstances and the best will in the world, this seems to be an appropriate use for calcium EDTA if you can keep the man under medical supervision. I have had a couple of supervisors in storage battery plants who have been hospitalized with not too devastating lead poisoning — and nobody would challenge the diagnosis — but they have got to go back, and on occasion they have got a new worker on the pasting machines. They have got to see about the ventilation. They have a lot of reasons for putting their breathing zone above safe limits of lead. Such people, I believe, may be submitted to one to four short courses of calcium sodium EDTA therapy by vein unless they are suffering from some renal damage.

The other group of patients who present problems are those with uncertain diagnoses of lead poisoning, and those we have already discussed. I have no hesitation in repeating these courses of EDTA by vein over and over again, for short periods at low dosage, with attention to laboratory studies of renal function. I don't think such treatment carries a hazard if it is given slowly in three-, four- or five-hour timed doses of the order of 1 gm to 2 gm, depending on the weight of the man.

DR. JOHNSTONE: Am I entirely wrong, and do I jeopardize the future of a patient, by merely withdrawing him from the environment? My daughters always said that all I know about therapy is to put a Band-Aid on the guy if there is something wrong on the outside, and give aspirin if there is something wrong on the

in my paper? Is the future of that man jeopardized in any way by not giving him EDTA? Is it justifiable to put a so-called minor case in a hospital and run up the expenses of giving him EDTA? In other words, is this whole philosophy wrong, of doing what we did before, believing physiological excretion was the fundamental thing, and should we go over to this EDTA almost routinely, eliminating the things you say about the kidney?

DR. HARDY: I certainly think that if a man has been exposed for ten or 15 years steadily to the inhalation of lead, some of it above the so-called safe limits, and if this is reflected in his blood findings, he can be said to have had intoxication. Each case is a case by itself, and anybody who suggests that EDTA be used routinely is, in my opinion, in error.

DR. THOMAS SHIPMAN: I want to agree with the things that Harriet has just said. In the early flush of our enthusiasm for using EDTA in treatment for various kinds of poisoning, there has been something of a tendency to play the numbers game. It is quite encouraging to see the excretion of lead or plutonium increased by a factor of 10 or 20 or 50, and everyone in the hospital stands around and cheers when those numbers come out.

The fact remains, I think, that perhaps we have made only a very small impression on the total body burden. This comes back to what Dr. Johnstone just said. Is he damaging the patient's chances by failure to give EDTA? I don't think so. I think that as far as lead is concerned, the great value of EDTA is in the relief of symptoms, and in tiding the patient over a temporary rough spot.

I would add one other very small point. Harriet mentioned that Harry Foreman demonstrated the kidney damage in animals. He demonstrated it in animals after we had already demonstrated it on a human, a case that was quite well worked up and the story published.

DR. W. C. WILENTZ: I am glad that Dr. Johnstone made some mention about the kind of case where you would use EDTA. First, I would like to give you my introduction to EDTA.

A representative of a company which sells it visited my office one day and wanted to know if I was using it. I told him no.

He said, "Why not?" I said, "Because of your magazine advertisement. I don't think it is a good thing. You have stated that it should be used prophylactically, as well as in lead poisoning itself. Until you change that, concerning its use prophylactically, I am not going to use it."

If you will look at the advertisement, you will see that it has been changed. They changed it about a month or so later.

There is one thing sure about the point of EDTA's use prophylactically, which was brought out here today, and that is, by giving EDTA you can produce a sense of false security. There is no question about it, and anything that will do that must be used cautiously.

What I have been interested in observing here today and yesterday was the question of what has happened to our calcium therapy. I am sure that is what Dr. Belknap had in mind. I think Dr. Kehoe would have that in mind, were he present this afternoon.

I have heard Dr. Shipman talk about relief of symptoms of lead poisoning, in the use of EDTA. Did you ever see anything so spectacular in your life as the relief of symptoms by giving intravenous calcium therapy? It is incredible. Nothing else has ever been manufactured that can give you that rapid, spectacular relief from symptoms. We have used calcium for years. There is no therapy that I know of that has been proved to be better than the old-fashioned calcium intravenous therapy.

Our results show it over the years. I have 75 to 80 lead intoxication cases right now. You can see my point of view. I am personally, from my own experience, still against delonding. I feel that it is safer, and more feasible, to let the delonding process take its natural course after you have gotten through with the acute stage.

I don't state that you can just ignore these men who are exposed. Somebody got the idea here that we are not treating these men. The doctors who spoke today didn't want to give anyone the idea that they are not treating these men when they say they are permitting them to excrete the lead naturally. I am sure none of you meant that, because you do treat them in your own particular fashion. And you get wonderful results.

I am still against delonding from what I have heard, particularly after what I have heard and read about EDTA.

I would like to ask one question of you, Dr. Hardy. Do you people in Massachusetts go entirely on porphyrin testing as to whether a man has lead poisoning or serious lead exposure? That is what I have been informed.

DR. HARDY: We are very much impressed with the level of porphyrin excretion in the urine as an index of the intoxication, not the exposure. That is the point. If you have a whole group of people in the storage battery plant who show a wide spectrum of lead values in urine, the porphyrin, we have found, when done quantitatively, gives a good idea as to who is going to turn up in the sick bay. I would like to quarrel with you about the use of calcium as therapy.

DR. WILENTZ: Porphyrin, of course, is not on the program, but I know men who work in lead plants who have large porphyrin excretions and have never gotten sick. Of course, I am only talking about porphyrin cases, where everything else is within normal limits.

DR. HARDY: I think we have come to a very good area of disagreement.

DR. WILENTZ: We have records to substantiate this fact.

DR. HARDY: A good healthy area. This is the area where we need more investigation. I challenge the concept that it is all right to let me walk around with indices of pathologic physiology, which is what a high porphyria is, whatever it is, because if it is due to alcohol — as Dr. Rozmiloff was saying yesterday and which has been shown years ago — then maybe something has to happen about that; but if you get it with low hemoglobin and you know the lead exposure. . . .

DR. WILENTZ: That is different.

DR. HARDY: That is?

DR. WILENTZ: That is different. That isn't what I asked you. If you get high porphyria excretions with other lead signs and symptoms, that is a different story. I can show you three or four dozen cases of high porphyrins, which we observed, that had no indications of symptoms or signs of lead intoxication. I am not talking about low hemoglobin, low blood counts, or high stippling cases.

DR. HARDY: You and I would have to set up the standards of lead intoxication so there is mutual agreement. My quarrel with you on calcium therapy rests on the fact that calcium forces the lead into the bony skeleton, rather than out of the body. And since there is a limit to the amount of lead that the skeleton can hold, unless the man is permanently removed from lead exposure, the risk of lead poisoning is increased. Am I not correct that forcing lead into the bone with calcium is the basis for its use as therapy?

DR. WILENTZ: Right.

DR. HARDY: The ionic lead goes into some form of phosphate and disappears in the. . . .

DR. WILENTZ: Mobilizes! Mobilizes the lead within the bony structure and takes the lead out of circulation, thus giving the body a chance to take a "breather" and prepare for the next stage, which is the excretion of lead by normal, natural metabolic and physiologic processes.

DR. HARDY. Dr. Johnstone wants to join.

DR. JOHNSTONE: I think, Harriet, you know a damn sight more about this than I do.

the gastrointestinal spasm, the metabolism. Don't forget that.

DR. HARDY: Our friend was saying he would rather use calcium and put the lead back in the bones. I am quarreling with that. I think we want the lead out.

DR. WILENTZ: It is excreted naturally thereafter, in a simple, painless and efficient process.

DR. HARDY: Do we take the man off the job?

DR. WILENTZ: There are not so many, not if your plant is really doing a job. You remove men when you have to, and watch the others as a precaution.

DR. HARDY: But with structural steel painters, for instance, there are many lead exposures where it is not simple to control the hazard. We are discussing a very complicated problem, and that is why, as you say, there is no easy prophylaxis, no routine handling, but each case is studied and treated as it occurs.

MR. CARL WALTERS: I would like to ask Dr. Hardy if she has been able to keep the intravenous injections of EDTA low enough in content to permit the men to continue on the job, or must they be hospitalized or taken off the job?

DR. HARDY: We insist on taking them off the job, for study of renal function and for intravenous treatment with EDTA.

MR. WALTERS: I know of some doctors who are dispensing the EDTA tablets orally and permitting the employees to continue working, but someone said yesterday they didn't approve of that. Do you approve of the oral administration of EDTA?

DR. HARDY: No. The effects, both good and bad, are not understood. Absorption through the gut of lead combined with EDTA is a possibility. Nobody really understands this. Maybe some lead gets into the blood as it comes through the intestinal wall.

Dr. Miller gave the same opinion for adult lead poisoning. Dr. Smith agreed for the children, and I hold the same view.

DR. BYERS: I spoke this morning of this, but it is such an impressive demonstration of what EDTA does, given by mouth with lead in the gut, that I think it is worth putting on the board.

We had a kid come in with mild lead poisoning, whose blood lead level we didn't get measured, but who had a fairly high coproporphyrinuria, about 250 to 300 micrograms per day, had stippled cells, had spinal fluid total protein of 80. Quite conscious. His lead output was measured for 24 hours; around 200 micrograms per 24 hours. At the end of this period, by mistake after the other. Within 24 hours, he was putting out 1,200 micrograms of lead per 24 hours in his urine. His spinal fluid total protein had gone up to 400. He was unconscious and in convulsions, and his coproporphyrin went way up beyond what we could measure. We then put him on intravenous EDTA and things calmed down, but he has been permanently damaged by this. That is, he had damage, which was not reversible, to the brain. I think this drug should never be given by mouth.

The other thing I would like to point out is that before we got into this mess, we were fussing with oral EDTA in children who had been treated because of lead poisoning, mostly with encephalitis, and we had gotten about a dozen children and were sure we had eliminated the lead from their homes. We put half of them on oral EDTA, a gram a day. The other half we left alone. No treatment at all, just following the urine qualitatively, seeing them in the hospital once in two weeks, doing a qualitative test for coproporphyrin. This group of children's coproporphyrin stayed positive anywhere from four to 17 months. These are the ones on oral EDTA.

The ones off EDTA ran coproporphyrins from four to 16 months, and certainly we didn't get rid of any more of the lead from them by this oral use of the drug, so that the oral use of the drug is ineffective as well as dangerous.

I have got to go, I am sorry to say. Thank you very much for letting me in.

CHAIRMAN BOWDITCH: Does that terminate this phase of the discussion?

If so, we come now to Mr. Waters' "A Lawyer Looks At Lead." Does anyone want to say anything more about that presentation? If not, we come to Dr. Baetjer's "The Effects of Season and Temperature on Childhood Plumbism."

Dr. Baetjer, would you like to add anything to what you said this morning?

DR. ANNA BAETJER: Dr. Shipman suggested at lunch that we test the effects of temperature on young animals. We have already performed experiments on both young and old animals, and we are doing more experiments. The age experiments are not yet complete enough to report.

CHAIRMAN BOWDITCH: We come now to the two papers on EDTA therapy, Dr. Miller's and Dr. Smith's. Are there any comments on these?

MR. F. P. MURPHY: I am not a physician, and I have been enlightened in the last two days and confused also. I would like to hear some other doctor's opinion on the use of EDTA in diagnosis that Dr. Hardy has brought out.

DR. R. F. BELL: It is possible that a provoca-

tive lead excretion study may be helpful in determining that a man has an excessive body burden of lead, when the usual lead studies do not reveal this burden. Until early 1955, we in Colorado believed, as most others, that a man did not have lead poisoning unless he showed excessive amounts of lead in his excretions and blood. Early in 1955, Dr. Sherman Pinto referred an unusual case to us for diagnosis and care, from a lead smelter plant located at 10,000 feet. This 36-year-old male, a Spanish-American, had over ten years of occupational lead exposure, and during the last eight years of that time he had had periodic urinary lead studies that varied in a normal range from 0.06 to 0.20 mg per liter corrected. For ten days prior to our seeing him, his own physician had given him 15½ gr of sodium thiosulfate intravenously daily, with no change in his complaining of loss of the working use of his hands, and numbness of his forearms and hands, of one month's duration. He denied, and we were unable to obtain, any past history suggestive of lead poisoning. Physical examination revealed dilatation of his left pupil, weakness of his left cheek, a minor lead line, gauntlet anesthesia to his elbows, loss of deep tendon reflexes in his forearms, weakness in his forearm supinators and pronators, and an inability to extend his wrists and fingers. Laboratory examinations showed a normal spinal fluid and normal kidney and liver function. This man showed a moderate hyperchromic anemia, with a hemoglobin of 11.75 gm. The expected normal, at 10,000 feet altitude is 17 gm. There was no basophilic stippling nor reticulocytosis. His white count was 13,700, with a normal differential. The blood lead was 0.07 mg per 100 gm, and his 24-hour urinary lead excretions were 0.08 mg per 24 hours, while his daily fecal lead excretions varied between 0.28 mg and 0.40 mg per 24 hours. Because of the typical neurological findings, anemia and history of lead exposure, we made a presumptive diagnosis of lead poisoning, in spite of the relatively normal body burden of lead as reflected by his blood, urine and fecal lead contents.

After four daily intravenous treatments of 3 gm of Ca EDTA, there was some return of his forearm deep-tendon reflexes, he could extend his fingers and wrists better, and his gauntlet paresthesia, inequality of pupils, facial paralysis and lead line had disappeared. During these four days of preliminary treatment he excreted 3.8 mg of lead. After three months of intermittent treatment, with a total of 60 gm of intravenous Ca EDTA and 42 gm of oral Ca EDTA, this man was clinically completely well and returned to his former work with no disability.

Since this case, several similar cases with normal range pretreatment lead studies have come to our attention and have been treated with Ca EDTA with equally gratifying results. One case was successfully treated with Ca EDTA in 1957, where in 1951 with the same complaints we had suggested, but had refused to make a diagnosis of lead poisoning because the patient's qualitative body fluid lead studies were within what we, as well as others, then considered normal limits. In these cases, with the dramatic remission of symptoms after Ca EDTA, the increase in lead excretion was also dramatic. It occurred to us that in certain cases, where relatively normal lead studies are found, with symptoms possibly compatible with lead intoxication, a provocative lead excretion study might be of value.

To do a 3 gm Ca EDTA intravenous provocative test and collect a 24-hour urine specimen is a little clumsy. When we studied the partitioned excretion of lead in a 24-hour period after using 3 gm, 1 gm, and 0.1 gm of Ca EDTA intravenously, we found that the cumulative percent of 24-hour lead excretion after the end of the intravenous infusion of Ca EDTA, between the limits of a 0.1 gm and 3 gm dose, followed a very reduplicatable curve equal to $72.4 \log t$, when t is the time from the end of the intravenous infusion in hours. A preliminary study of the increased amount of lead excreted after a provocative test with 0.1 gm, 1 gm, and 3 gm, was in the ratio as 1 is to 1.8 is to 3.3 times, respectively. This means that 3.3 times as much lead will be excreted in the urine of any particular individual after 3 gm of Ca EDTA as will be excreted after 0.1 gm intravenously.

We studied individuals with lead symptoms and a history of exposure, and compared their excretions with several normal subjects with no symptoms or history of lead exposure, before and after treatment with Ca EDTA. In the lead-exposed cases, the ordinary 24-hour urinary excretions of lead often overlapped the normal studies, but a distinct separation of the exposed and non-exposed groups could be determined from the amount of increased 24-hour lead excretion after 3 gm of Ca EDTA. From these studies we have tentatively decided that if the increase in the 24-hour urinary excretion after 3 gm of Ca EDTA intravenously is more than 1.2 mg, then it is presumptive that the individual has more than a normal increase in his body burden of lead. If the increase is less than 0.62 mg, then he presumptively does not have an abnormal increase in lead body burden. Comparatively this means that after 0.1 gm of Ca EDTA intravenously, which can easily be given from a syringe and rather rapidly, an

tive.

You can see that with the 24-hour cumulative percent curve, a provocative test can be easily performed in an office under controlled supervision. A man wastes his urine in a bottle and immediately is given 0.1 gm Ca EDTA in 10 cc of water intravenously, and the exact time noted. The patient then does not void again for three to six hours, and the three- to six-hour specimen is collected and the exact time recorded under direct supervision. The amount of lead found in this specimen is then corrected to 24 hours on the cumulative percent curve for his 24-hour excretion.

In conclusion, we believe that a provocative excretion study is of value under certain circumstances, but that considerable study and corroboration are needed before it can be accepted as a criterion in lead surveys or diagnosis. One word of caution — we have found that if there has been recent treatment with Ca EDTA, our provocative criterion fails. A four- to six-week treatment-free period should be allowed to elapse before evaluating a provocative study.

Before closing I would like to say a word in defense of the treatment of lead poisoning with Ca EDTA. We have been afforded the opportunity to supervise the treatment of nine cases of inorganic lead poisoning in adults with what we previously assumed were permanent neurological changes, and have seen miraculous recoveries after treatment with Ca EDTA. One of these cases had forearm extensor weakness, wrist-drop and other neurological disturbances for 20 years while remaining out of exposure without improvement; and after one and a half years of intermittent Ca EDTA treatment he recovered normal function. This man was being retired as totally disabled, supposedly with CNS loss, at the time we first saw him, but was returned to normal work after his treatment with Ca EDTA. He had unrecognized complicated lead poisoning, not CNS syphilis.

We have seen severe colic relieved by Ca EDTA when calcium gluconate, morphine, Demerol and Dilaudid have given no relief of pain. We have seen a case of hyperchromic anemia, fatigue, weakness and vague joint pains from lead reversed within days after Ca EDTA therapy, yet the patient had formerly failed to respond, after removal from exposure to lead for about a year and treatment by several excellent internists with liver, B_{12} and iron. After a short period of daily intravenous treatment, this case was later given oral Ca EDTA by his physician, and immediately developed a one plus albuminuria which cleared after four months. His kidney

than that one instance of temporary albuminuria that developed after oral Ca EDTA, we have not seen any adverse effect from two- to eight-week intermittent treatment with four or five daily intravenous 3 gm doses, nor from the sporadic experimental use of daily 3 gm oral Ca EDTA. We have given several hundred treatments with Ca EDTA since 1952. Some individuals in our group, with neuropathies, have been treated intermittently for as long as two years.

MR. WALTERS: Could I ask you, were all these men hospitalised, or non-working?

DR. BELL: All the men with neuropathies, except one, were hospitalised during their original study and treatment. After partial recovery they were followed on the job, and hospitalised only intermittently every month or six weeks for several days of treatment and study.

CHAIRMAN BOWDITCH: I think this brings us to the end. We have already had the discussion of the final paper, the one by Dr. Kehoe, and all that is left is Dr. Shipman's summation. Does anyone wish to summarise the summation?

MR. WALTERS: I don't want to summarise the summation, but there are some things I would like to ask. I am a layman and not a doctor, although I have been closely associated with lead-exposed persons for about 32 years. Back in 1943, a committee of the most reputable men in their field in the United States published a marvelous book called "Occupational Lead Exposure and Lead Poisoning." I don't know where the responsibility lies for getting out a new and revised edition of this authoritative booklet, but until standardised techniques and limitations are set up, we are going to continue to have diverse opinions and diverse papers.

I hope that some day the Lead Industries Association will take it upon itself to publish a booklet by the experts so that others who are not so well informed may readily refer to expert diagnostic methods of evaluating lead absorption and the various accepted techniques for determining lead in air, lead in blood, lead in urine, porphyrin values, and so on. But to educate the entire world, of course, is a big order for the lead industry.

CHAIRMAN BOWDITCH: There is no such thing as getting all the doctors to agree on these changes. It can't be done. Is there anything further?

MR. WALTERS: Work towards that end.

DR. SHIPMAN: If no one else summarises the summary, perhaps for the sake of the record I would like to do it myself; and perhaps anticipate the 1968 meeting. There are certainly areas of ignorance in the field of lead toxi-

cology, and it seems to me that the works which we will be hearing about ten years from now will involve a continuation of the general studies on lead physiology and lead toxicology, studies such as those described by Anne Baetjer and Bob Kehoe today. We certainly would hope that ten years from now we will have more precise laboratory tests for exact determination of the degree of lead poisoning, and certainly we have reason to hope that, ten years from now, we will know more about the biological effects of small doses of lead. The fact that exposures and blood and urine levels are kept below a certain point does not guarantee that damage isn't being done, damage which we are still unable to determine.

Now this is not anything directed only at lead. The same thing is true in a wide variety of fields. As I said at lunch, the ideal exposure is zero. Somewhere between zero and what we might call permissible levels, there is an area which requires study, and I would hope that this will be a topic on the agenda in 1948.

CHAIRMAN BOWDITCH: I declare the conference at an end, and I thank you all for making it such a success.

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at

LEAD HYGIENE CONFERENCE

November 6-7, 1958

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