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June 24, 1961

Malcolm H. Merrill, M.D., Director
State Department of Public Health
2151 Berkeley Way
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California

Dear Malcolm:

I am directing to your attention a few critical remarks relating to the article on "Lead Poisoning in Industry", which I received a day or two ago from your Department, under the heading Occupational Health, technical information service. I send these to you for two reasons, one being that I do not know who prepared the article; the other is that I do not wish to take any one of your group "over the coals". What I have to say is meant to be constructive criticism, and it is so crucial to the proper application of certain measures of industrial hygiene in the lead trades, that it must, I believe, be said with all the vigor that it deserves.

I have not had the time to go over every part of the statement carefully, and I have not considered this necessary. What has been said on a number of matters is not what I would say, nor is it said in the manner in which I would say it. That is of little importance, for no two people see things quite the same or speak of them in the same manner. There are two points, however, that deal with quantitative data and relationships in which one is either right or wrong, and in this instance incorrect statements are made.

(1) The first of these occurs under "Coproporphyrinuria", in which the flat statement is made that "a high degree of correlation has been - - demonstrated between coproporphyrin (concentrations) and urinary or blood levels." This is not as bad as it seems at first, but actually it is not true. The concentration of coproporphyrin in the urine does not vary with the extent of the absorption of lead or with its rate of excretion in the urine or with its concentration in the blood; it tends to increase abruptly when the level of absorption exceeds the critical point of danger, whereas it remains within normal limits at all safe levels of lead absorption. It is a sign, not of absorption of lead, but of interference with a normal function of the body, and hence it denotes intoxication. It does vary somewhat in degree with the severity of the intoxication, but not necessarily with the extent of absorption of lead. What is said in the article is not altogether untrue at the higher levels of absorption, but it is misleading, especially because it confuses the issue in industrial hygiene by using a sign of intoxication as a sign of danger after the fact. What one says here has to be said carefully, and from precise knowledge.

(2) More serious errors are the statements concerning lead in the

blood. "It is well established that clinical signs and symptoms of lead intoxication may exist with levels below 0.08 mgm per 100 grams." This is not strictly untrue, but what the author of this statement means is untrue, as is shown by the sentences that precede and follow it. For example "The upper limit of normal for blood lead is 0.08 mgm/100 gm whole blood"---. This is a flatly incorrect statement. The concentration of lead in the blood of normal persons in the United States rarely exceeds 0.05, and never exceeds 0.06 mg. per 100 grams. The latter level is found so rarely as to be regarded as the result of a greater than usual analytical deviation. Much, of course, depends upon the analytical procedure, but a properly carried out procedure need not be in error by more than ± 0.01 mg. per 100 grams of whole blood, in dealing with quantities of 10 grams of blood. The concentration of 0.08 mgm per 100 grams of whole blood is an absolutely critical one. I have never seen a single case of lead poisoning in a child or an adult at the time of onset of intoxication, whose blood level was below 0.08 mg. per 100 g., and I believe I can say without any possibility of doubt, that we have checked this point by more observations than has anyone else in this country or elsewhere, and by methods of analysis that are of high and known accuracy. Symptoms may persist after the concentration of lead in the blood has diminished, and therefore, if the sick person is not investigated early in the disease, it may happen that the concentration in the blood is as low as 0.06 mg. per 100 grams. The fact as I have stated it, is of the greatest importance, however, in industrial hygiene, for if an individual is removed from work just before the threshold level of 0.08 has been reached, he does not develop lead intoxication. You will recognize, therefore, that I am not dealing with an academic point, but with a highly significant fact which has been put to crucial test in practice for a period of years. On this point the entire medical regimen of industrial hygiene in the lead trades depends for its certainty that it can recognize danger before any illness of any kind develops. In the tetraethyllead industry we have to depend solely upon the urine instead of the blood, (for the metabolism of TEL in the body is such that the concentration in the blood is no index of the concentration in the body). The principle is the same, however, although the practice differs somewhat.

I would appreciate it if you would call these matters to the attention of your people. I do not expect them to alter or retract these statements, at present, but they should know that they are incorrect. In due course, if the matter comes up, I shall have to take issue with such statements. These are not the only misstatements on the record, however, and they will not be the last. The recent book of Johnstone and Miller contain the astonishing misstatement that the threshold of danger, with respect to the concentration of lead in the blood is 0.10 mg. per 100 grams. Where they got this figure, I have no idea, but I have chided them about it. These things will be straightened out in time, and my only reason for referring this to you is to make such corrections as easy as possible rather than as difficult as it may become if some one's feelings get hurt!

With best personel regards.

Sincerely yours,

Robert A. Kehoe, M. D.

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WE BELIEVE THE ATTACHED MATERIAL
WILL BE OF INTEREST TO YOU

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Occupational Health



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LEAD POISONING IN INDUSTRY

Fatal lead poisonings have progressively declined over the past thirty years in many industries, but control of the lead hazard is still unsatisfactory. During the year 1959, twenty-nine cases of lead poisoning were reported to the Bureau of Occupational Health, California Department of Public Health. It is probable that many more cases remain unreported and many were not recognized. Methods of complete control of the lead hazard are well known so that, ideally, no case of lead poisoning should occur, yet nonfatal lead poisoning is a common systemic occupational disease. Some of this is from the unwitting use of lead compounds in new processes, but exposure is known to be possible in more than a hundred different kinds of industries, including smelting, refining, lead reclaiming, battery manufacture, outdoor painting with lead based paints, pottery glazing, welding and soldering, metalizing, and ship scrapping.

ROUTES OF ABSORPTION

Lead is taken into the body by inhalation, by ingestion, and, rarely, through the intact skin. By far the greatest number of cases in industry are from inhalation of lead dust and fumes, since relatively insoluble lead compounds may be dissolved in the lungs and absorbed through the respiratory mucous membranes. At present, tetraethyl lead as found in gasoline is the only widely distributed form of lead capable of being absorbed through the skin. Cases of poisoning from tetraethyl lead have been reported, but fortunately are rare because strict industrial hygiene controls are enforced by the tetraethyl lead industry, and because the concentration in ordinary gasoline is so low as to present little or no hazard to handlers, such as truckers, service station attendants, and

others. (Tetramethyl lead has been added recently to gasoline as a substitute for tetraethyl lead but the amount of lead is about the same.)

TYPE OF POISONING

1. Acute Poisoning: This form usually results from the ingestion of large amounts of lead salts, commonly the acetate or subacetate. In industry, however, this form of acute lead poisoning is relatively rare. It does occur occasionally from exposure to tetraethyl lead or lead fumes. The ingestion of lead salts produces signs and symptoms including a metallic taste, vomiting, severe colic, and constipation or bloody diarrhea. Central nervous system symptoms predominate in tetraethyl lead poisoning and include insomnia, mental irritability and instability as early significant findings. These may be followed by headache, convulsive movements, frank convulsions, and death.

2. Chronic Poisoning: This is the most frequent type of lead poisoning. For descriptive purposes the signs and symptoms may be classified as early and late manifestations.

Early - The onset of chronic lead intoxication is frequently insidious with headache, weakness, lassitude and constipation, followed soon by the pain of intestinal colic. A lead line along the gum margin may be present; this is one indication of lead absorption, but not necessarily of intoxication. These early symptoms are by far the most common presenting complaints of lead poisoning.

Late — If the patient fails to heed the early warning symptoms and exposure continues, nervous manifestations sooner or later develop. These frequently begin with nervousness, tremors, weakness of the extensor muscles — particularly those of the hands and forearms — and sensory disturbances, including paresthesia and anesthesia. Eventually extensor paralysis may develop, with obvious wrist or foot drop. Severe chronic poisoning may be followed by symptomatic involvement of the central nervous system, as with acute poisoning. Fortunately, encephalopathy is relatively rare, occurring usually after exposure to tetraethyl lead, or nonoccupationally in children who ingest leaded paint from furniture or walls. In the acute state, there is excitation and confusion which may be followed by stupor with or without convulsions, coma, and death. In the chronic type of severe lead poisoning, involvement may occur with insomnia, vertigo, personality changes, and visual disturbances.

HISTORY

Accurate differential diagnosis requires a careful systems review to rule out appendicitis, acute gastroenteritis, renal colic and other causes of abdominal pain which may simulate lead colic. Numerous disorders of the nervous system may be confused with the peripheral neuritis or encephalitis of lead poisoning. Such diseases include poliomyelitis and other infections, central nervous system neoplasms, and poisoning from toxic substances other than lead.

Particularly important is the occupational history of the patient. Points to consider are previous and present exposure to specific jobs, duration of exposure, presence or absence of symptoms in other workers, and time of onset of symptoms in relation to occupational exposures.

PHYSICAL EXAMINATION

Although none of the signs are pathognomonic of lead poisoning, the most commonly occurring are as follows:

1. Pallor: This is probably a manifestation of inadequate peripheral circulation and may or may not be associated with anemia.
2. Weakness and paralysis: This occurs mainly in the extensor muscles of the wrist. Early stages can be detected by excessive fatigability of these muscles when they are exercised.

There may be no objective evidence of general muscular weakness, so that the striking feature of the condition is the discrepancy between the muscular development of the patient and his apparent lack of strength when tested. True wrist drop or other paralysis is a relatively uncommon occurrence.

3. Gingival lead line: Believed to be due to a deposit of lead sulfide; this sign appears as a grayish black series of dots most easily seen along the gum margin with the aid of a good magnifying glass. A good occupational history can differentiate a lead line from lines caused by other heavy metals.

LABORATORY DATA

A diagnosis of lead intoxication cannot be made by laboratory examination alone. The laboratory supplements the history and physical examination.

Hematology — Anemia due to lead poisoning is normocytic in type and usually not severe. Defective erythrocytes are common, however, and polychromatophilia, basophilic stippling, poikilocytosis, and anisocytosis may all be found in the peripheral circulation. Demonstration of all these abnormal cells may require multiple smears.

Basophilic stippling of the erythrocytes is the principal significant finding in the blood. When determined by an experienced technician from a carefully prepared smear, this finding has diagnostic significance. Polychromasia is often closely associated with basophilic stippling and may be observed in the same cell.

Stippled erythrocytes are not pathognomonic of lead poisoning but represent a reaction of bone marrow to a toxic substance. Their value is enhanced by periodic examination of the blood to observe changes in the proportion of stippling. In cases of known lead exposure stippled cells in excess of 12 cells per 50 oil immersion fields are suggestive of excessive lead absorption.

Urinary Lead - Although day to day variation in urinary volume is relatively large, values of lead when corrected for specific gravity, correlate fairly well with the quantity of lead absorbed. The procedure for collection of urinary samples from lead workers must be meticulous since there is always the possibility of contamination by lead from clothing or skin, or from glassware, or the surrounding atmosphere. Twenty-four hour samples are preferred over spot samples for accuracy. Normal lead excretion varies from 0.01 mg to 0.08 mg/liter in large samples of over one liter. Spot samples (50 ml or more) vary from 0.05 to 0.12 mg/liter. Increasing values above 0.15 mg/liter indicate excessive lead absorption; however, concentrations considerably in excess of 0.15 mg/liter have been found in the absence of significant evidence of lead poisoning. As a rule of thumb, however, one may anticipate signs and symptoms of lead intoxication as the urinary lead concentration exceeds this value. Urinary lead determinations require exacting analytical procedures and, therefore, require the services of a competent chemical analyst.

Coproporphyrinuria - The presence of porphyrins in the urine occurs in a number of diseases, especially those of the liver and blood. Alcohol and barbiturates are examples of intoxicants which may also markedly elevate urinary porphyrins. Such toxic or diseased states must be considered in the differential diagnosis; however, in the known lead worker a frank 4+ test for coproporphyrinuria is most likely to indicate approaching lead intoxication. In lead intoxication porphyrinuria is usually more marked than in other disorders and is often demonstrable before basophilic stippling of red cells is observed. A high degree of correlation has been satisfactorily demonstrated between quantitative coproporphyrin values and urinary or blood lead levels.

Blood Lead - The analysis of blood for lead is specific and is generally considered to correlate more closely with a clinical diagnosis of lead poisoning than do urinary lead determinations. The analytical procedures, however, are as exacting and time consuming as those for urinary lead. The upper limit of normal for blood lead is given as 0.08 mgm/100 gm whole blood, and concentrations in excess of this are indicative of excessive absorption, and therefore objectionable exposure. Values from 0.06 to 0.08 are considered a transition zone and amounts below 0.06 are normal for persons with no exposure to lead.

It is well established that clinical signs and symptoms of lead intoxication may exist with levels below 0.08 mgm per 100 gm blood, and conversely, evidence of intoxication may be absent when blood lead concentrations are quite high. For these reasons the diagnosis of lead poisoning requires much more than a laboratory procedure.

Blood lead concentrations are less variable than urine values. The risk of contamination of sample is much less than with urine samples since the blood must be collected by a trained technician or physician.

THERAPY

Rational treatment of lead poisoning first requires that all lead exposures be temporarily terminated. Cases with mild symptoms and no disability may often require no treatment other than removal from exposure and medical observation. In such instances the source of the excessive exposure should be determined and corrected immediately.

Abdominal cramps are best relieved by intravenous injection of 10 cc of 10 percent solution of calcium gluconate repeated every three to four hours as necessary for pain. When the diagnosis of acute surgical abdomen has been definitely ruled out, constipation may be relieved by the administration of one ounce of magnesium sulfate daily. This also helps remove whatever lead may be present in the gastrointestinal tract.

Anemia, if present, is not of the iron deficiency type and the administration of iron is unnecessary. A high protein, high vitamin diet is desirable, however.

In cases presenting wrist drop, a cock-up splint, to include the fingers, worn day and night, is used until function returns. Gentle massage every day or two and hot water baths are used. Strenuous exercises or massage should be avoided.

In cases of lead encephalopathy, sedation may be required. For convulsions, barbiturates are effective — sodium amobarbital 0.25 to 0.5 gm may be given intravenously, for example. Lumbar puncture may be required to relieve increased intracranial pressure. In severe cases neurosurgical decompression may be indicated.

EDTA Therapy (Edathamil) — Ethylene-diamine-tetra-acetic acid is a sequestering chelating compound capable of combining with lead, calcium and other multivalent cations to form a non-ionized (sequestered), ring-type (chelated) complex. The administration of EDTA or its sodium salts to man or animals results in the chelation and elimination of calcium with consequent hypocalcemia. To avoid this, the calcium disodium salt of EDTA is used. Lead ions will replace calcium in the complex because of the greater stability of the lead complex. The lead complex is highly soluble in aqueous solutions, is non-ionized and readily excreted by the kidney. This bound lead being non-ionized does not exert its characteristic toxic effects. EDTA and its salts increase urinary lead excretion in plumbism by as much as twenty times, and hence, are effective "deleading" agents.

The toxicological potential of these compounds, however, is not fully understood and several patients with plumbism treated with EDTA have died of renal disease, attributed to the use of the drug. The use of EDTA and its salts should be reserved for those cases of plumbism that fail to respond satisfactorily to established therapeutic measures, and then only when kidney function studies indicate the absence of renal disease. Such studies should be done concurrently with the administration of EDTA.

With EDTA it is possible to appreciably increase the excretion of lead, but the results of this cannot necessarily be predicted. In many

patients there has been dramatic subjective improvement occurring shortly after treatment is begun. In other cases symptoms persisted without significant change. The recommended maximum dose for administration intravenously of edathamil calcium disodium is 0.17 gm per hour, 0.33 gm per day, or 1.67 gm per week for each 10 lbs. of body weight. The administration of EDTA by mouth as a substitute for adequate industrial hygiene control of lead exposure is certainly to be condemned as both irrational and dangerous.

PREVENTION AND CONTROL

There are three essential features of an adequate program for control of an atmospheric health hazard:

1. Provision of adequate environmental control to prevent exposure of the worker to contaminated air and to provide facilities for maintaining high standards of personal cleanliness.
2. A program of instruction aimed at (1) alerting the workers to the need for maintaining high degree of personal cleanliness, and (2) instructions of the worker in the proper operational procedures which will result in minimum environmental exposures.
3. A medical program that is adequate to detect early evidence of overexposure so as not only to prevent poisoning but provide a check on the effectiveness of the protective devices provided.

These three features may function in a number of ways. The following are examples:

1. Adequate environmental control
 - a. Sources of lead contamination can be eliminated or reduced by "designing in" control features in the original structure or machinery.
 - b. All operations which might disperse lead dust or fume should be enclosed as much as possible. Such operations as material conveying, mixing or grinding, can often be performed within complete enclosures.

- c. Where complete enclosure is not possible, local exhaust should be provided. Local exhaust systems must act largely by controlling the motion of the contaminated air. The important considerations in this type of ventilation control are: (1) collection of the contaminated air in as concentrated a form as possible, and (2) provision of sufficient transport air velocity to convey the contaminant to suitable disposal equipment.
 - d. Lead fumes from heated lead pots, particularly above 700° F., should be controlled by local exhaust in an upward direction to take advantage of the natural convection air currents.
 - e. Good housekeeping is essential to prevent the accumulation of lead dust. The amount of dustiness which is contributed to the air by the continual redissemination of settled dust is sometimes more than 50 percent of the total dust concentration. Such dust can be removed from floors and surfaces by industrial vacuum systems or portable vacuum cleaners and/or wetting down for subsequent waste disposal.
2. Personnel instruction on proper operating procedures and good personal hygiene.
- a. Workers handling lead-containing materials should be provided with and required to use adequate washroom facilities to prevent ingestion of lead compounds. Since smoking can be a significant cause of lead inhalation, it should be restricted to uncontaminated areas.
 - b. Respiratory protective devices, if provided, should be approved by the California Division of Industrial Safety or the U.S. Bureau of Mines for protection against lead dust or fumes. Since unclean or faulty respirators can cause a false sense of security, responsibility for their maintenance, repair, and cleanliness should be jointly shared by management and the employee. Many companies find it feasible and useful to have workers turn in a used respirator at the end of each shift, so that they

can be reissued a cleaned and reliable respirator at the beginning of the next shift. It should be remembered that respirators are acceptable only where the control of the environment is not possible, or where the exposure is for short periods of time. There are very few operations that cannot be satisfactorily controlled by good industrial hygiene engineering design, so that respirators should be used only as a temporary and secondary expedient.

- 3. The education of the worker for his own protection is fully as important as the prevention of dispersal of dust and fumes. He must be told the proper way to perform his job; he must be informed of the protective devices built in or provided for his protection; and he must be sold on the value of avoiding high concentrations of lead dust.
- 4. A physician should supervise the health of the employees, including the making of periodic examinations and performing laboratory work. Lead-affected workers found at these examinations should be transferred to nonhazardous jobs within the plant, there to recover under physician's supervision. They should not be allowed to return to their former occupation until the hazard has been eliminated.

The foregoing recommendations have been directed at reducing atmospheric contamination and in securing medical data to be used as a source of information to indicate where improved environmental control should be applied.

The presently accepted maximum concentration which may be tolerated by employees for an eight hour working day, is 0.2 milligram of lead, or any of the lead compounds, per cubic meter of air. Experience has shown that exceeding this figure in most cases will lead to excessive lead absorption, if not to lead poisoning.

It is believed that a majority of plants in which lead is used in some way will endorse such a control program. To the few who may dissent, we must point out that continued failure to meet the accepted standards for the protection of

workers in the industry can result only in undesirable effects on the worker, the industry and the community. It can be stated with almost certainty that a forthright and constructive

approach to the problem will result in improved morale and efficiency of workers and will actually result in savings to the industry.

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