1935

The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 104, NO. 2 CHICAGO, ILLINOIS JANUARY 12, 1935

EPIDEMIOLOGY OF LEAD POISONING

A. J. LANZA, M.D.

Assistant Medical Director, Metropolitan Life Insurance Company

NEW YORK

The use of lead is so widespread throughout all civilized countries that lead poisoning continues to be a matter of concern to the physician and the public health official. As new processes are evolved in industry and new materials devised for general consumption, so does lead poisoning continue to appear under new and sometimes strange circumstances. For centuries the origins of lead poisoning, its nature, its varied forms, the action of lead in the body, the treatment and the prevention of lead poisoning have all occupied the men of science and the men of industry and the last word has not yet been spoken.

Lead poisoning may well be thought of as a counterpart of syphilis not only in the variety of its effects on the human system but in the manner in which it may be dormant and unsuspected in the tissues for years, apparently innocuous, until some alteration in the metabolic processes liberates it with unimpaired venom. Like syphilis, it is a contributing cause of many a death for which it does not receive its rightful share of the blame.

Lead may gain entrance to the body through the respiratory system by inhalation, through the gastrointestinal system by ingestion, and through the skin. It is doubtful whether skin absorption of inorganic lead compounds ever takes place except when the skin is damaged by inflammation or wound. While cases have been reported due to the application of lead-containing medication to ulcerated or damaged skin, this form of entry is of little practical interest. Organic lead compounds, such as tetra-ethyl lead, will penetrate the skin and their employment is guarded by carefully devised precautions.

Recently Fairhall and Heim[1] published the results of their study of lead weighted silk fabrics and found no evidence of absorption even when the fabric was worn next to the skin and under extreme conditions of activity and perspiration.

Inhalation and ingestion are the two routes by which lead gets into the system, and the first is the more important. Most of the industrial exposure arises from dust and fumes that are breathed into the lungs and upper respiratory tract, where absorption and excretion involve entry into the systemic circulation. Lead that is ingested may be excreted unchanged and, even if absorbed, may be carried to the liver and excreted in the bile.[2] In the main, industrial poisoning is due to inhalation and nonindustrial poisoning to ingestion, though there are, of course, exceptions.

Water supplies conducted through lead pipes have been an important source of community poisoning. In a study of 102 lead-conducted water supplies in New England, 24 per cent of 253 individuals examined were found to be lead poisoned. This study indicated that the greater the carbon dioxide content of the water, the more readily lead was carried into solution. The authors of this investigation concluded that the daily ingestion of 0.1 mg. of lead over a period of eight and one-fourth years caused poisoning.[3] In the Bulletin of the United States Public Health Service for July 28, 1932, the statement is made that "No water to be used for drinking purposes should contain the equivalent of one-half part lead per million water." An English study showed that the infant mortality in an area exposed to lead-contaminated water fell from 134 to 56 when the water was treated to prevent the lead going into solution.[4] Epidemics of lead poisoning from water supplies have been reported from England,[5] France,[6] Germany[7] and other countries.

Numerous instances have been reported both in this country and in England of lead poisoning due to home fermenting and distilling of wines, beers, ciders and similar beverages in utensils glazed with a lead compound. As with water, the acid content of these beverages causes the trouble; the resultant chemical action liberates the lead from the glaze and it goes into solution in the beverage.[8]

Other interesting and important epidemics of poisoning have occurred from time to time to bear witness to the ubiquity of lead and to the strangeness of the circumstances under which it may manifest itself. A series of cases of lead poisoning was reported from Austria in 1931. Lead was used to counterbalance a grinding wheel in a flour mill, with the result that the flour was impregnated with fine particles of metallic lead, poisoning a number of people.[9] The use of snuff has been identified with lead poisoning, the source of the lead being the metallic foil in which the snuff is wrapped.[10]

Read before the Section on Preventive and Industrial Medicine and Public Health at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 13, 1934.

1. Fairhall, L. T., and Heim, J. W.: J. Indust. Hyg. **14**: 317 (Nov.) 1932.
2. Aub, J. C.; Fairhall, L. T., and others: Medicine **4**: 1 (Feb.-May) 1925.
3. Wright, W.; Sappington, C. O., and Rantoul, E.: J. Indust. Hyg. **10**: 234 (Sept.) 1928.
4. Milligan, Ernest: Brit. M. J. **2**: 222 (Aug. 1) 1931. Ingleson: Action of Water on Lead, Technical Paper No. 4, Water Pollution Research, Dept. Sc. Ind. Res., London, His Majesty's Stationery Office, 1934.
5. University of Aberdeen Report, Lancet, December 1933.
6. Thouvenet, cited in Chronic Poisoning from Water in Lead Pipes, Paris letter, J. A. M. A. **97**: 654 (Aug. 29) 1931.
7. Kruse and Fischer: Bull. Hyg. **6**: 74 (Jan.) 1931.
8. Willcox, R. L.: Brit. M. J. **2**: 222 (Aug. 1) 1931. Wright, Sappington and Rantoul.[3]
9. Berger, W.; Studeny, O., and Rosegger, F.: Wien. klin. Wchnschr. **45**: 586 (May 6) 1932.
10. Beck, A. A.: Bull. Hyg. (abstr.) **8**: 679 (Oct.) 1933.

One of the strangest occurrences was lead poisoning in a number of Baltimore families caused by the use of discarded storage battery cases for fuel.[11] There were forty cases with several of severe encephalopathy among the children. A similar instance in Nashville, Tenn., involved five families and fourteen children.[12]

One of the most interesting of all the chapters on lead poisoning is that dealing with ocular neuritis among children. In 1897 Dr. Lockhart Gibson of Queensland, Australia, published a paper on this subject, referring to two previous reports in 1892.[13] Dr. Gibson followed up this subject for forty years, reporting cases and endeavoring to trace the source of infection. The general conclusion was that the Queensland cases were due to lead paint on verandas and railings where the children played.[14] Recently similar cases have been described in this country.[15] In Japan, the use of lead-containing toilet powders has caused widespread lead poisoning in both infants and mothers.[16]

It is not possible to describe or even to enumerate, in a paper of this length, all the varied industrial processes in which lead is used and the circumstances wherein lead poisoning may arise. Their number is legion.

Unfortunately, also, there is but little statistical information on the mortality from lead poisoning and none with respect to morbidity. In no year since 1920 have there been as many as 150 cases of death from lead poisoning reported in the registration area of the United States. In 1930 there were 101 cases; in 1931, 111. Half of the 1930 patients were painters.[17] These reports are based on death certificates, and there is no doubt that many cases of lead poisoning are reported as nephritis or other organic diseases, with no mention of the underlying cause. The Joint Occupation Study [18] (a life insurance undertaking) showed, for house painters, on the basis of 61,000 life years, 249 actual deaths from all causes, which was 22 per cent in excess of the expected. This excess was reckoned on the basis of ordinary policyholders, corrected for age groups and sex. Aside from this meager information, there is little worth recording.

The following summary refers to the main classification of industries and processes in which lead is a hazard:

1. Lead mining when lead is in the form of soluble carbonates or other soluble salts. It is doubtful whether any appreciable amount of lead poisoning occurs when the ore is galena (lead sulphide).
2. Lead smelting and refining.
3. Handling and fabrication of metallic lead:
   (*a*) Manufacturing of lead articles of all kinds (poisoning due to formation of lead oxide on surface of metallic lead).
   (*b*) Handling metallic lead in hot processes, lead burning, soldering, lead tempering, plumbing.
   (*c*) Brass and other founding in which lead is used.
   (*d*) Buffing and polishing metallic surfaces in which lead is an ingredient.
4. Manufacture of lead salts and compounds, especially lead oxide by Dutch method, Carter method, and other methods; lead pigments; organic lead compounds.
5. Manufacturing processes in which lead compounds are used. These are extremely numerous; among the important ones are the storage battery industry, paint industry, glass industry, rubber compounding and chemical industry.
6. Application and removal of lead-containing paints, enamels and glazes. Painting, spray painting, vitreous enameling, pottery dipping, sandpapering, scraping and chipping painted surfaces; flame cutting of painted metal; tree spraying with lead-containing insecticides.
7. Typographic trades: type founding, electrotyping, stereotyping.

It may be said that in those industries in which lead plays a major part the hazard is fairly well controlled, and it is exceptional nowadays to see cases of acute poisoning with colic and wrist drop in the smelters and establishments where lead oxide, paints and storage batteries are manufactured. There is still in these industries a considerable amount of mild lead poisoning, much of which escapes diagnosis because it is mild. Individual carelessness and breaks in the discipline of supervision do occur, and familiarity breeds contempt in the dangerous trades as elsewhere. Much credit, however, is due the lead industries for the perfection of a technic of prevention and supervision, which is, in the main, effective. When one comes across an outbreak of lead poisoning it is usually in an establishment in which a lead process is but one step in the plan of manufacture, as it is under such circumstances that the hazard is apt to be underestimated or ignored. Moreover, it is not uncommon to see lead poisoning among industrial workers not engaged in handling lead but who, through negligence, are exposed to dust or fumes from lead processes not properly isolated or otherwise protected.

Some time ago I had occasion to visit a plant where one process consisted in soldering brass strips. These strips were assembled by girls working at long tables and passed to the man at one end of the table, who did the soldering. The prevailing air currents carried the fumes from the lead pot along the table, affecting the girls, while the solderer escaped any ill effect. Some of these lead poisoning cases will cause the medical Sherlock Holmes to exert his best faculties in detecting the source of contamination. A notable example was contributed by Dr. Leathers of Nashville, Tenn.[19] In this instance, in the vitreous enameling of domestic heaters, a lead-free pigment was used. A number of acute cases of lead poisoning developed, including individuals not associated with the enameling process. It finally developed that there was lead in the glass frit used in making the enamel. As this had not been realized, no precautions were taken. Numerous cases of lead poisoning have been reported due to cutting metal coated with lead paint, with the oxyacetylene flame, especially in the holds of naval vessels and similar confined spaces. Here again the poisoning was not limited to the men actually doing the cutting.[20]

A great deal of effort has been expended in endeavoring to ascertain the amount of lead present in the atmosphere under varying conditions and the minimum dosage that will cause lead poisoning. Bloomfield[21] reported that in a number of industrial establishments he found 0.10 mg. of lead to 10 cubic meters of air

11. Williams, Huntington; Schulze, W. H.; Rothschild, H. R.; Brown, A. S., and Smith, F. R., Jr.: Lead Poisoning from the Burning of Battery Casings, J. A. M. A. **100**: 1485 (May 14) 1933.
12. Crutcher, J. S. Jr.: J. Tennessee M. A. **26**: 20 (Jan.) 1933.
13. Gibson, J. L.: Australian M. Gaz., Oct. 20, 1897; M. J. Australia **2**: 201 (Sept. 8) 1917, and **1**: April 1, 1922.
14. Gibson, J. L.: British J. Ophth. **15**: 637 (Nov.) 1931.
15. Vogt, E. C.: Roentgenologic Diagnosis of Lead Poisoning in Infants and Children, J. A. M. A. **98**: 125 (Jan. 9) 1932. McKhann, C. F.: Lead Poisoning in Children, Am. J. Dis. Child. **32**: 386 (Sept.) 1926. Metropolitan Life Insurance Company, statistical bulletin, vol. 11, No. 10.
16. Kato, Katsuji: Lead Meningitis in Infants, Am. J. Dis. Child. **44**: 569 (Sept.) 1932.
17. Hoffman: Lead Poisoning Legislation and Statistics, Newark, N. J., Prudential Press, 1933.
18. Joint Occupation Study, 1928 (Actuarial Society of American and Association of Life Insurance Medical Directors).
19. Leathers, W. S., and Morgan, H. J.: The Study of Lead Poisoning in an Enameling Plant, J. A. M. A. **89**: 1107 (Oct. 1) 1927.
20. Stitt: U. S. Navy M. Bull., April 1912. Brown, E. W.: J. Indust. Hyg. **8**: 113 (March) 1926.
21. Bloomfield, J. J., and Isbell, H. S.: J. Indust. Hyg. **15**: 111 (May) 1933.

in automobile repair shops, 0.13 mg., and in street air, 0.09 mg. to 10 cubic meters. Greenburg [22] has reported that 1.45 mg. of lead daily for two and one-half years has caused poisoning. Teleky [23] states that 1 mg. of lead daily for several months and Legge and Goadby [24] state that 2 mg. daily for several years will cause lead poisoning. While these figures may seem to vary considerably, it is true that lead in the form of vapor is more dangerous than as dust, and the circumstances under which the foregoing estimates were determined were not identical. Certainly it may be concluded that a daily dosage of from 1.5 to 2 mg. is distinctly hazardous and eventually will cause poisoning in most, if not all, individuals. In this connection it should be noted that when lead is in a molten condition fumes will be given off; the higher the temperature, the more fumes; also oxide will form on the surface and get into the air as dust.

CONCLUSION

It may be stated that lead poisoning is very prevalent, though most of it is mild. However, both mild and occasionally severe cases are commonly not recognized. Many cases are diagnosed as chronic appendicitis and even as gallbladder disease, with all too frequent surgical intervention. In connection with industrial hygiene studies, insurance company records show that, with respect to illnesses of more than seven days' duration among wage earners, respiratory diseases greatly outnumber gastro-intestinal diseases. When the ratio is inverted and one is confronted with a situation wherein the gastro-intestinal cases outnumber the respiratory cases, the possibility of lead poisoning should always be considered.

THE BIOCHEMICAL BEHAVIOR OF LEAD IN THE BODY

JOSEPH C. AUB, M.D.
BOSTON

In the last ten years, a great deal of work has appeared bearing on the biochemistry of lead. To combine this new knowledge with that summarized in a previous publication [1] is my purpose in this article.

In regard to absorption there is little important new evidence. The experience in industry confirms what has been found in the laboratory [1]—that lead which is inhaled is far more toxic than lead which is swallowed. Of course, it is likewise generally conceded that ingested lead is a hazard.

The form in which lead is transported in the blood stream is of practical as well as scientific interest, as it has a bearing in guiding intelligent therapy. The prevailing opinion had long been that lead was carried as an albuminate, but Fairhall's equilibrium experiments,[1] as well as our blood studies with Reznikoff,[1] convinced us that lead was precipitated in the bones as the very insoluble tertiary lead phosphate and carried in the blood as the more soluble di-lead phosphate. To this view Brooks [2] agreed, but Maxwell and Bischoff [3] and recently Kehoe and Thamann [4] have objected, largely on the basis that lead in the blood stream reacts more with red blood cells than does the phosphate. Maxwell and Bischoff [3] have produced some evidence that lead, when injected intravenously, is carried as a diphosphoglycerate, while Jowett [5] thinks that it forms a complex inorganic phosphate with calcium and chlorine. In a chemical system as complicated as blood plasma, an equilibrium of several such chemical compounds is not unreasonable. Any of these compounds might remain ionized and dispersed in the presence of plasma proteins. But whether it is transported as an inorganic or organic phosphate, it is obvious that lead in the blood stream can exert deleterious effects on body cells.

Of course, some absorbed lead is probably excreted (partly in the urine but mostly in the feces) without ever having been stored. There is a growing accumulation of data obtained by different chemical technics that indicate a small daily lead excretion in the urine in the vast majority of the people in this country and elsewhere.[6] The average result of these observations indicates a urinary excretion of lead of from 0.05 to 0.1 mg. daily in individuals with no unusual lead exposure. This urinary excretion represents lead that has been actually absorbed, but a large percentage of the lead found in the feces has probably never even been absorbed. Because of such repeated observations it must now be agreed that a qualitative demonstration of small quantities of lead in the excreta does not necessarily signify abnormal exposure. According to Barth,[7] a very small amount of lead may even be gradually accumulated in normal bones during advancing years (from 0.02 mg. found in infancy to 0.1 mg. per 3 Gm. of bone ash in the aged).

If larger quantities of lead are inhaled, swallowed or injected, excretion does not maintain an equilibrium, and lead becomes stored. But the extent of possible storage can be ascertained best when a known quantity of lead is injected intravenously. Millet,[8] Kehoe and Thamann,[9] and Aub and Smithwick [10] have shown that but little of this is excreted promptly. For example, the average of six of our cases, studied for forty-six days during the injection period, showed that only 69 mg. of lead was excreted in both the urine and the feces, although 473 mg. of lead as colloidal phosphate was injected intravenously.

22. Greenburg, L.; Schaye, A. A., and Shlionsky, H.: Pub. Health Rep. **44**: 1666 (July 12) 1929.
23. Teleky, L.: Arch. f. Gewerbepath. u. Gewerbehyg. **5**: 132-137, 1933.
24. Legge and Goadby: Lead Poisoning and Lead Absorption, London, Edward Arnold; New York, Longmans Green & Co., 1912.

Read before the Section on Preventive and Industrial Medicine and Public Health at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 13, 1934.

1. Aub, J. C.; Fairhall, L. T.; Minot, Anne S., and Reznikoff, Paul: Lead Poisoning, Medicine Monographs, Baltimore, Williams & Wilkins Company **7**, 1926.
2. Brooks, John: The Interaction of a Finely Divided Lead Suspension with Blood Serum, Ringer Solution and Aqueous Phosphate Solution, Biochem. J. **21**: 766, 1927.
3. Maxwell, L. C., and Bischoff, Fritz: The Reaction of Lead with the Constituents of the Erythrocytes, J. Pharmacol. & Exper. Therap. **37**: 413 (Dec.) 1929.
4. Kehoe, R. A., and Thamann, Frederick: The Behavior of Lead in the Animal Organism: III. Colloidal Lead Compounds, J. Lab. & Clin. Med. **19**: 178 (Nov.) 1933.
5. Jowett, Maurice: The Reaction of Lead Compounds with Serum and Serum Models, Biochem. J. **26**: 2108, 1932.
6. Badham, C., and Taylor, H. B.: Lead Poisoning, extract from the Report of the Director-General of Public Health, New South Wales, for the year ended 31st December 1925. Kehoe, R. A.; Edgar, Graham; Thamann, Frederick, and Sanders, Lester: The Excretion of Lead by Normal Persons, J. A. M. A. **87**: 2081 (Dec. 18) 1926. Fretwurst, F., and Hertz, A.: Quantitative Determination of Lead in Feces and Urine and Its Significance in the Diagnosis of Lead Poisoning, Arch. f. Hyg. **104**: 215, 1930. Litzner, S., and Weyrauch, F.: Untersuchungen über den Bleigehalt des Blutes und Harns, seine Beziehungen zum Auftreten klinischer Krankheitserscheinungen sowie seine diagnostische Bedeutung, Arch. f. Gewerbepath. u. Gewerbehyg. **4**: 74, 1932. Kehoe, Robert; Thamann, Frederick, and Cholak, Jacob: On the Normal Absorption and Excretion of Lead: I. Lead Absorption and Excretion in Primitive Life, J. Indust. Hyg. **15**: 257 (Sept.) 1933.
7. Barth, E.: Investigation of the Lead Content of Human Bones, Virchows Arch. f. path. Anat. **281**: 146, 1931.
8. Millet, H.: The Excretion of Lead in Urine, J. Biol. Chem. **83**: 265 (Aug.) 1929.
9. Kehoe, R. A., and Thamann, Frederick: The Behavior of Lead in the Animal Organism: II. Tetra-Ethyl Lead, Am. J. Hyg. **13**: 478 (March) 1931; footnote 4.
10. Aub, J. C., and Smithwick, R. H.: Lead Treatment of Cancer, New England J. Med. **208**: 310 (Feb. 9) 1933.