SPECIAL PROBLEMS OF LEAD IN WOMEN WORKERS

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A B S T R A C T

Women workers may be more susceptible to lead toxicity than men, and they developed more central nervous system manifestations than men. The incidence percentage for convulsions and blindness was greater among women than men.* Also, lead may affect the reproductive capacities in women since incidence of miscarriage is greater among occupationally exposed women workers.# Lead was found to cross the placenta in experimental animals and may affect developmental growth and behavior of newborns. Compounds used in therapy may have potentiating toxic effects. In experimental studies, lead was found to potentiate the toxic effects of lithium on the fetal liver, as well as Chang human liver cell cultures.

The major symptoms of lead poisoning have been described many years ago. These symptoms include loss of appetite, metallic taste in the mouth, constipation, anemia, and pallor. Weakness, insomnia, headache, and nervous irritability have been described as other manifestations in lead toxicity. There also could be muscle and joint pain, fine tremors, encephalopathy, and abdominal colic. The muscle weakness may progress to palsy, often observed as "wrist-drop" or "foot-drop."[1-2-3-4]

The exposure of the worker to lead could occur through several routes, namely ingestion, inhalation, or through the skin. In women workers this hazard could be increased, since long hair can become contaminated with lead dust.[5]

When absorbed lead reaches the blood, it is predominately associated with the erythrocytes.[6] However, the manner in which the lead is associated with the erythrocytes is not well understood. It has been postulated that lead in erythrocytes cannot be removed by dialysis. The lead remains in the cells and is only slowly exchanged with lead in the plasma.[7] The concentration of lead in blood is considered more useful for toxicological evaluation than lead in the urine because of the dilution fluctuation which occurs in urine lead.

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**Percentages: Convulsions, men 15.0, women 34.9; blindness, men 2.3, women 7.7.*
#Three times as great in pre-maritally exposed women workers.

There are no data which correlate the concentration of lead in blood and that in other tissues of the same person.[3] The difficulties in this type of approach are due to the distribution of the body burden of lead in exchangeable pools. There have been studies which correlate the level of blood lead to the lead in the air. Goldsmith and Hexter[8] were able to show a linear correlation between the amount of lead in the air and the concentration of lead in the blood of people exposed to environmental lead pollution.

Lead interferes with heme synthesis and disturbs the formation of hemoglobin.[2,4,9] This might produce anemia and deposition of lead in the bone marrow of the fetus where depression of heme synthesis in the mother's cells could also contribute to the production of anemia. The intermediate substrate, delta-aminolevulinic acid (ALA), has been found to increase with increased lead exposure. As lead interferes with delta-aminolevulinic acid dehydratase (ALAD), the enzyme necessary for heme synthesis, the inhibition of such an enzyme is accompanied by an increase of the substrate, ALA. Both ALAD and the substrate, ALA, have been used as parameters in determination of exposure to lead. Blood levels of the enzyme and substrate, or urine levels of the substrate, are sometimes utilized in determining the amount of exposure to lead.

The cardiovascular system could be affected indirectly by increased levels of lead due to interference with blood hemoglobin levels and eventually diminished capacity for oxygen saturation. It has been shown that hypertension among workers in the lead industry correlates with lead exposure. These hypertensive crises could lead to rupture of cerebral vessels and eventually to brain damage and paralysis.

The oxidative enzymes in the retina could be inhibited by lead, leading to cases of total or incomplete blindness. As lead is deposited in different organs, the end result of toxic manifestation is dependent upon the damage to such target organs.

The approach to discussion of the problem of lead in women workers can be considered from the following points:

1. Are women more sensitive to lead than men?
2. Does lead affect their reproductive capacity?
3. Does lead cross the placenta and affect the fetus?
4. Is there any synergistic effect of lead with other therapeutic drugs?

To discuss the first question, there are no current data which can show six differences in sensitivity to lead. However, as was mentioned above, blood lead levels have been used to correlate exposure to airborne lead and the rate of uptake. Table I shows blood lead levels of several selected populations. This table shows the mean of blood lead level in µg/100 ml of blood was 26 µg. Most of these analyses have been done by less sensitive techniques than are available in testing today.

TABLE I

BLOOD LEAD LEVELS OF SELECTED POPULATIONS

Type of population	Mean Blood Lead µg/100 ml
Cincinnati Policemen	25
Cincinnati Traffic Officers	30
Cincinnati Automobile Test Lane Inspectors	31
Cincinnati Garage Workers	31
Los Angeles Traffic Policemen	31
Boston Summer Tunnel Employees	30

Adapted from Publication #999-Ap02, January, 1965
United States Department of Health

Table II shows blood lead levels of selected populations exposed to the same environmental conditions, but categorized as mean blood levels for women and men in µg/100 ml of blood. It is shown that women in any of the types of occupations studied had a much lower blood lead level than men having the same environmental exposures. This observation has been noted by several workers, however, no proper explanation for the differences has been given.

In the University of Illinois Medical Center Hospital, such differences between men and women have been shown to exist with regard to

lead levels.* In these two studies, there was no correlation between air levels of lead exposure to that of blood lead levels.

TABLE II

BLOOD LEAD LEVELS OF SELECTED POPULATIONS

Type of Population	Mean Blood Lead µg/100 ml	
	Men	Women
Remote California - Mountain	12	9
Composite Rural United States	16	10
Suburban Philadelphia	13	13
Composite Urban United States	21	16
Los Angeles Aircraft Workers	19	17
Pasadena City Employees	19	12
Downtown Philadelphia	24	18

Adapted from Publication #999-AP02, January, 1965
United States Department of Health

It has been shown that a linear correlation exists between exposure to lead in air and the rate of uptake as manifested by blood lead levels.

Comparisons of the blood lead content among men and women with correlation to an environmental lead level. These data suggest that there is greater accumulation of lead in target organs among women

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**Information obtained from a personal communication.*

than among men. Urine lead can be used to evaluate the rate of excretion of lead from the blood.

Men and women workers have been divided into three groups, those having a low exposure, intermediate exposure, or high exposure to lead, see Table III.

TABLE III

COMPARISON OF URINE AND BLOOD LEAD CONTENT AMONG MEN AND WOMEN UNDER SAME EXPOSURE

GROUP EXPOSURES	Urine Lead Content		Blood Lead Content	
	Number Analyses	Average µg/liter±S.D.	Number Analyses	Average µg/100±S.D.
LOW				
Men	146	35 ± 21	148	26 ± 11
Women	123	28 ± 19	124	26 ± 10
INTERMEDIATE				
Men	102	43 ± 30	108	30 ± 11
Women	25	27 ± 15	27	22 ± 10
HIGH				
Men	386	88 ± 60	329	44 ± 16
Women	61	46 ± 25	58	34 ± 13

Adapted from Neal, P. A., et al, Public Health Bulletin 267, Washington, D.C., GPO, 1941

At any of these levels of exposure the mean blood lead level among women was much lower than the mean among men similarly exposed. Also, the urine content was lower in women than men. This suggests that, although women were exposed to the same lead levels as men, their rate of excretion of lead was lower and their blood lead levels were lower than those found in men. By this comparison, it can be further suggested that lead in women has a different distribution pattern than in men and that lead in women may be stored in organs at higher concentrations than in men, when both are exposed to the same environmental conditions.

If one accepts this hypothesis, one might expect some target organs to show different stages of injury among women that do not correspond to what happens in men. Table IV lists some incidences of clinical lead toxicity among men and women.[10] These data date back to several years ago, at which time a recent study was not available. The fact is, women were not allowed to work in lead industries prior to 100 years ago. However, the trend today is for women to work in the same occupational areas as men, which might tend to produce more nearly identical exposures in

women and men who have been exposed to the same environmental conditions.

TABLE IV

INCIDENCE OF SOME CLINICAL PICTURES OF LEAD TOXICITY AMONG MEN AND WOMEN

TOXIC MANIFESTATIONS	INCIDENCE PERCENT	
	Men	Women
COLIC	77.6	69.8
PARALYSIS	57.0	30.0
CONVULSIONS	15.0	34.9
BLINDNESS - TOTAL	2.3	7.7
BLINDNESS - PARTIAL	3.5	10.2

Adapted from Pendergast, W. D., British Medical Journal, 1:1164, 1910[10]

From the limited data listed above, we can deduce that women workers are more sensitive to lead exposure than men because of the amount of lead in the blood in women exposed to the same level of environmental lead is much lower than that found in men. Also, the excretory rate of lead among women is lower than the rate in men exposed to the same level of environmental lead.

In dealing with the second question, "Does lead affect the reproductive capacity in women?" Lund,[11] has shown that there is an effect of lead on the reproductive capacity of women. In this research, it was found that the number of productive pregnancies were abnormally small among women previously exposed to lead in their occupations. This has been commented on by Hamilton, Oliver, Lane, Cantarow, and Trumper.[12-5-3] On the other hand, the Wentachee Study in 1941,[13] had shown that exposure to low lead levels in the air had no effect on fertility, either in men or women. However, women workers are exposed to higher lead levels than environmental lead. Several studies have shown that lead affects the reproductive organs in animals.[14-15-16]

From the above presentation, it is desirable to suggest that women at the stage of reproduction should not be exposed to high levels of lead.

The third problem facing us is the effect of lead on the unborn fetus. There have been several animal studies which show that the lead can cross the placenta.[14-15-17] Table V lists some lead levels in fetal or newborn blood of different animal species, as well as in humans exposed to ambient levels of lead.

TABLE V

MATERNAL-FETAL "STEADY STATES" FOR LEAD

MATERNAL DOSE OR CONCENTRATION OF LEAD			SPECIES	CONCENTRATION OF LEAD IN FETUS OR NEWBORN
Diet	µg/g		Rat	µg/g
	0.61			0.56
	64.0			4.2
	512.0			23.4
I.V.	µg/ml	time	Rat	µg/g
	705.0	1 hour		6.0
	1080.0			53.0
I.V.	µg/ml		Rat	µg/g
	50.0	6 hours		0.3
I.V.	µg/ml		Mouse	µg/g
	30.0	6 hours		0.02
I.V.	µg/100ml	20 min.	Goat	µg/g
	26.0			25.0
Ambient	µg percent		Human	µg/100 ml
	14.0			11.0*
				µg/g
	(6-26)			100.0#

* *Cord Blood (4-24)*

\# *Rib at Term*

During pregnancy, exposure of pregnant animals to a high level of lead was accompanied by abortion. This has also been shown in several clinical observations, among women workers in the lead industry. In the battery industry, among pregnant women workers having blood lead levels ranging from 30 to 80 µg/100 ml of blood, several cases of abortion were reported. The effects of lead on the fetus may be due to the necrotic effect and disturbance in the fetal blood supply which results in abortion.

If the placental membrane is of the lipoid nature with high levels of phospholipids, as in the brain, one may expect a one-way movement of lead from the maternal to the fetal side.

In some of our studies,[17-18-19-20] concentrations of lead injected into pregnant animals were accompanied by concentrations of lead in the fetus up to 10 times higher than the maternal blood levels. This may represent a selective transport of lead from maternal to the fetal side. However, with exposure of pregnant animals to higher lead concentrations, abortions occurred with only 60 percent of lead in fetal blood, compared to the maternal blood level. The protein binding capacity of lead may play a role in such cases of high blood lead levels.

Exposures of pregnant mice to different low levels of lead chloride were accompanied by complete development of the litters and normal delivery.[20] However, the litters did not show normal growth rate over a 35-day period, as expressed in weight gain in grams. See Fig 1.

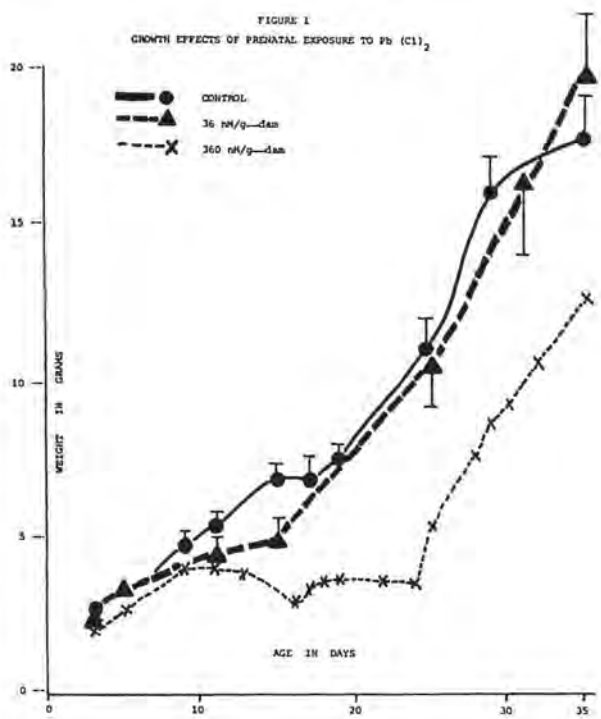

Figure 1 Growth Effects of Prenatal Exposure to Pb $(Cl)_2$

Another study was conducted on the litters with regard to motor activity development in post natal life. Figure 2 represents the effect of low concentrations of lead on the motor activity of litters born from

mothers injected with different lead levels, as well as that of controls. As is shown at the end of a 10-day period, the experimental group were very close to the controls; however, as litters developed in age, motor activity was more affected. Litters from mothers exposed to 360 nm of lead had much lower motor activity than those of control mothers or mothers injected with 36 nm of lead.

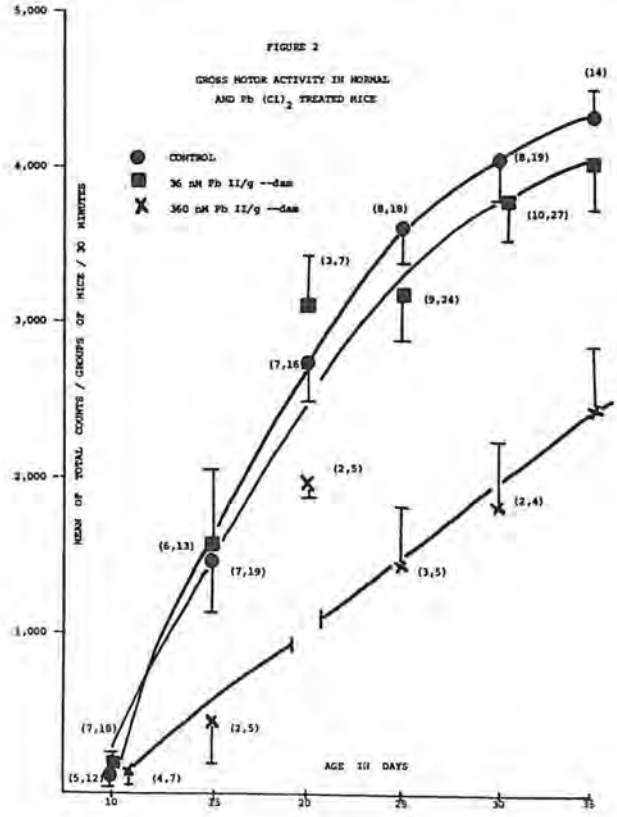

Figure 2 Gross Motor Activity in Normal and Pb $(Cl)_2$ Treated Mice

So the hazardous effects of lead on the fetus could be summarized as the occurrence of abortion with high exposures and, when litters were not aborted, a much lower rate of growth as well as diminished motor activity developed.[20]

The last point to be considered in this presentation will be the question of exposure of women workers to drugs, in addition to their exposure to lead. The synergistic effect of lead has been studied in animals and in *in vitro studies*.[17-21] The combined injection of lead and lithium in pregnant animals were accompanied by much higher damage to fetal liver than exposure to either compound alone. Tissue cluture of human liver cells (Chang cells) were used to determine such an effect. The determination of some leakage of lysosomal enzymes as β-glucoronidase and lactic dehydrogenase were determined for cultures

where lead alone, boron alone, lithium alone, or any of the combinations were added. The levels of β-glucoronidase and lactic dehydrogenase were higher in cultures exposed to any of the three elements than the control where no element was added. The increase was more than double in combinations of lead and lithium, the increase in the enzymes were mainly additive. As lithium is used a a psychotherapeutic agent, women workers exposed to lead while undergoing such therapy, may experience increased toxic effects. Also, both lithium and lead cross the placental membrane and more hazardous effects on the fetus could be expected[17,21].

In conclusion, more research is needed to determine safe levels of lead which will not result in harmful health effects in women of child bearing age. Pregnant women are at high risk to lead exposure which can also affect fetal development. Recent studies indicate that men working in the lead industry have a higher rate of abnormal children, which suggests that the reproductive system in males is affected by lead. It is important to establish a low safe level for lead in the industrial environment which will protect both men and women in the work place during their reproductive years.

REFERENCES

1. Bell, W. B., Williams, W. R., and Cunningham, L., The toxic effects of lead administered intravenously, Lancet, 2:793, 1925

2. Berk, P. D., Tshcundy, D. P., Shepley, L. A., Waggoner, J. G., and Berlin, N. I., Hematologic and biochemical studies in a case of lead poisoning, Amer J Med, 48:137, 1970

3. Cantarow, A., and Trumper, M., Normal Intake of Lead in Lead Poisoning, The William and Wilkins Co., Baltimore, 1944, p. 167

4. Chisolm, J. J. Jr., Disturbances in the biosynthesis of heme in lead intoxication, J Pediat, 64:174, 1964

5. Lane, R. E., The care of the lead worker, Brit J Ind Med, 6:125, 1949

6. Bult, E. M., Nusbaum, R. E., Gilmore, T. C., and Didio, S. L., Trace metal levels in human serum and blood, Arch Environ Health, 8:52, 1964

7. Clarkson, T. W., and Kench, J. R., Uptake of lead by human erythrocytes *in-vitro*, Biochem J, 69:432, 1958

8. Goldsmith, J. R., and Hexter, A. C., Respiratory exposure to lead: epidemiological and experimental dose-response relationships, Science, 158:132, 1967

9. Feldman, F., Lichtman, H. C., Oransky, S., Ana, E. S., and Reiser, L., Serum d-amino levulinic acid in plumbism, J Pediat, 74:917, 1969

10. Prendergast, W. D., The classification of the symptoms of lead poisoning, Brit Med J, 1:1164, 1910

11. Lund, C., The effect of chronic lead poisoning of reproductive capacity, Nord Hyg Tidskr, 18:12, 1936

12. Hamilton, A., Lead poisoning in pottery file works and porcelain enameled sanitary ware factories, U. S. Bureau of Labor Statistics, Bulletin 104:56, 1912

13. Neal, P. A., Dressen, W. C., Edwards, T. E., Reinhart, W. H., Webster, S. W., Castberg, H. T., and Fairhall, L. T., A study of the effect of lead arsenate exposure on orchardists and consumers of sprayed fruit, Public Health Bulletin 267, Washington, D. C., U. S. Government Printing Office, 1941

14. Cheatum, E. L., and Benson, D., Effects of lead poisoning on reproduction of mallard drakes, J Wild Managmt, 9:26, 1945

15. Dalldorf, G., and Williams, R. R., Impairment of reproduction in rats by ingestion of lead, Science, 102:668, 1945

16. Ferm, V. H., and Carpenter, S. J., Developmental malformations resulting from the adminstration of lead salts, Exp Molec Path, 7:208, 1967

17. Boulos, B. M., Carnow, B. W. Naik N., Bederka, Jr. J. P., Kauffman, R. F., and Azarnoff, D. L., Placental transfer of lithium and enviromental toxicants and their effects on the newborn, Fed Proc, 32:2989 1973

18. Boulos, B. M., Almond, C. H., Davis, L. E., and Jackson, R. L., Placental transfer of diazoxide and its hazardous effect on the newborn, Fed Proc, 29:665, 1970

19. Boulos, B. M., Almond, C. H., Davis, L. E., and McKenzie, J. W., New surgical technique for studying placental transfer of drugs *in-vivo*, Amer J Surg Res, 10:7, 1970

20. McLellan, J. S., Von Smolinski, A. W., Bederka, J. P. Jr., and Boulos, B. M., Developmental toxicology of lead in the mouse, Fed Proc, 33:289, 1974

21. Boulos, B. M., Interaction between lithium and lead toxicities, Galinsini, 19:257, 1974

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