

## LEAD AND $\delta$ -AMINOLEVULINIC ACID DEHYDRATASE LEVELS IN MATERNAL AND CORD BLOOD

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### Abstract

Lead concentrations in 50 samples of umbilical cord blood and 66 samples of maternal venous blood during the labor were determined. Among them, 47 pairs of maternal and cord blood specimens were included.

The average lead levels for maternal and cord blood in 47 pairs were found to be 7.5  $\mu\text{g}/\text{dl}$  and 6.6  $\mu\text{g}/\text{dl}$  respectively. The average values of hematocrit and hemoglobin levels in maternal blood were significantly lower than those in cord blood. A close correlation was found between lead concentrations in maternal and cord blood ( $r=0.85$ ). A good correlation was observed between  $\delta$ -aminolevulinic acid dehydratase (ALA-D) activities in maternal and cord blood ( $r=0.58$ ). A certain negative correlation was observed between blood lead levels and logarithm (log) of ALA-D activities in maternal blood ( $r=-0.29$ ), however, no consistent association was observed between blood lead levels and log ALA-D activities in cord blood.

### INTRODUCTION

As a result of growing industrial use of lead and the introduction of alkyl lead compounds as petroleum additives, environmental pollution by lead has come to be a subject of increasing concern<sup>1)</sup>. Many epidemiological and experimental data on the concentration of lead in the air and that in the blood of exposed populations suggested that, in man, lead can accumulate as a result of increasing environmental contamination of lead<sup>2)</sup>.

There is also considerable experimental<sup>3)</sup> and clinical evidence<sup>4,5)</sup> that lead can readily transferred across the placenta from maternal to fetal circulation and accumulates in the fetal tissues<sup>6)</sup>. The fetus is considered to be most susceptible to lead toxicity, especially during the stage of most active growth<sup>7)</sup>, however, the effects of chronic exposure to lower levels of blood lead (Pb-B) in the fetus are largely unknown.

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Many authors have reported that ALA-D activity in blood was one of the most sensitive and specific indicators of low level lead effect. They also reported the existence of a good negative correlation between ALA-D activity and the concentration of lead in blood, even within the "normal" range of Pb-B concentration<sup>8,9,10,11</sup>.

Thus, it would be reasonable to expect that ALA-D activity might have been diminished *in utero* at these "normal" Pb-B levels, while there are no data available in the literature for this relationship.

This report concerns the relationship between Pb-B levels and ALA-D activities in maternal and cord blood from women at delivery, in order to assess the risk of low level lead toxicity in the population of fetuses and infants, without known abnormal lead exposure.

#### MATERIALS AND METHODS

During the period of 13 months from June 1976 through June 1977, 66 samples of maternal venous blood during the labor and 50 samples of umbilical cord blood from the infants immediately after delivery were obtained. Among them, 47 pairs of maternal and cord blood specimens were included. Almost all of the mothers had lived in the suburbs of Kurashiki City during gestation, and were following and delivered by the same group of obstetricians in the same hospital. They represented uncomplicated and full term deliveries. None of the mothers had a history of increased lead exposure nor cigarette smoking. The age of the mothers ranged between 19 and 37 years (mean 27 years).

Approximately 2 ml of blood specimens were obtained in lead free plastic disposable syringes and placed in lead free tubes coated with heparin-Na (Wako). The concentration of lead in the blood was determined with an atomic absorption spectrometer (Perkin-Elmer 503) equipped with a deuterium background corrector and a graphite furnace (Perkin-Elmer HGA-2000). Whole blood was diluted ten-fold with Triton X-100 (2g/l) and 15  $\mu$ l of the diluted samples were directly injected into HGA-2000, according to the slightly modified method described by Fernandez, F. J.<sup>12</sup>. Erythrocyte ALA-D activity was assayed by the method of Tomokuni, K.<sup>13</sup>. The hemoglobin (Hb) content was measured as cyan-methemoglobin and the hematocrit (Ht) reading was determined by the micro-capillary method.

#### RESULTS

The Pb-B levels, ALA-D activities, Ht values and Hb contents in 66 samples of maternal and 50 samples of cord blood are shown in Table 1.

TABLE 1. Hematological parameters in maternal and cord blood

		Maternal blood	Cord blood
Pb-B*	$\mu\text{g/dl}$	$7.6 \pm 3.3$	$6.5 \pm 3.8$
ALA-D**		$1.41 \pm 0.33$	$1.22 \pm 0.27$
Hematocrit	%	$38.5 \pm 4.5$	$48.7 \pm 6.4$
Hemoglobin	$\text{g/dl}$	$12.8 \pm 1.7$	$16.3 \pm 2.2$
Number of samples		66	50

\* Lead concentration in blood, Mean  $\pm$  S.D.

\*\*  $\delta$ -aminolevulinic acid dehydratase  $\mu\text{mol PBG/hr/ml RBC}$

The similar data of Pb-B, ALA-D, Ht and Hb levels in 47 pairs of maternal and cord blood samples (24 male infants and 23 female infants) are summarized in Table 2. As shown in Table 2, the average lead levels in maternal blood and cord blood were  $7.5 \pm 3.4$  and  $6.6 \pm 3.8$   $\mu\text{g/dl}$  respectively. The median of maternal blood lead was 6.1  $\mu\text{g/dl}$  with a range of 2.5 to 19.5, and

TABLE 2. Hematological parameters in the paired samples of maternal and cord blood

		Male <sup>a)</sup>		Female <sup>b)</sup>	
		Maternal blood	Cord blood	Maternal blood	Cord blood
Pb-B*	$\mu\text{g/dl}$	$7.1 \pm 3.5$	$6.1 \pm 3.6$	$8.0 \pm 3.3$	$7.2 \pm 4.1$
ALA-D**		$1.41 \pm 0.26$	$1.17 \pm 0.30$	$1.53 \pm 0.39$	$1.30 \pm 0.23$
Hematocrit	%	$38.8 \pm 3.7$	$49.1 \pm 7.2$	$37.3 \pm 4.0$	$48.6 \pm 5.9$
Hemoglobin	$\text{g/dl}$	$13.1 \pm 1.2$	$16.5 \pm 2.2$	$12.4 \pm 1.6$	$16.2 \pm 2.3$
Number of samples		24		23	

		Total	
		Maternal blood	Cord blood
Pb-B*	$\mu\text{g/dl}$	$7.5 \pm 3.4$	$6.6 \pm 3.8$
ALA-D**		$1.47 \pm 0.33$	$1.23 \pm 0.28$
Hematocrit	%	$38.1 \pm 3.9$	$48.9 \pm 6.5$
Hemoglobin	$\text{g/dl}$	$12.7 \pm 3.9$	$16.4 \pm 2.3$
Number of samples		47	

\* Lead concentration in blood

\*\*  $\delta$ -aminolevulinic acid dehydratase  $\mu\text{mol PBG/hr/ml RBC}$

a) Samples from male infants and corresponding mothers

b) Samples from female infants and corresponding mothers

the median of cord blood lead was 4.4 with a range of 1.9 to 19.2  $\mu\text{g}/\text{dl}$ . This difference was not statistically significant. The average Ht value and Hb content in the maternal blood were significantly lower than those in the cord blood. There were no statistically significant difference between the Pb-B, ALA-D, Ht and Hb values found in the pregnant mothers at term and in their newborn offsprings.

The frequency distribution of Pb-B levels for the maternal and cord blood samples of 47 pairs are shown graphically in Fig. 1. The same data are plotted on logarithmic normal probability paper in Fig. 2. The data on Pb-B in maternal and cord blood have been found to follow log-normal distribution rather than normal distribution.

The frequency distributions of ALA-D activity in maternal and cord blood are shown in Fig. 3. The same data are plotted on normal probability paper in Fig. 4. As shown in the figures, the data on ALA-D activity in maternal and cord blood seemed to follow normal distribution rather than log-normal distribution.

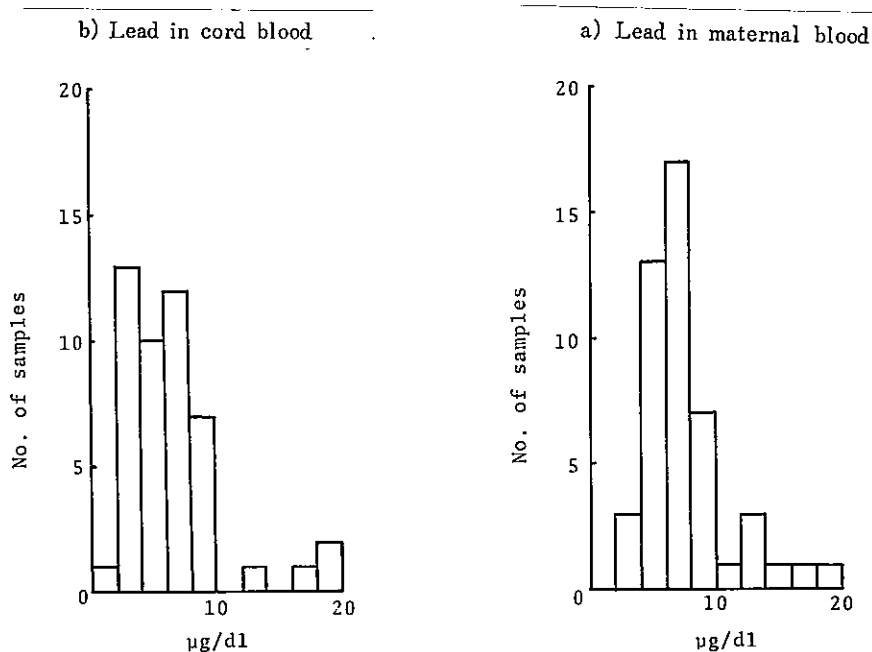


Fig. 1. Frequency distribution of lead levels in maternal and cord blood

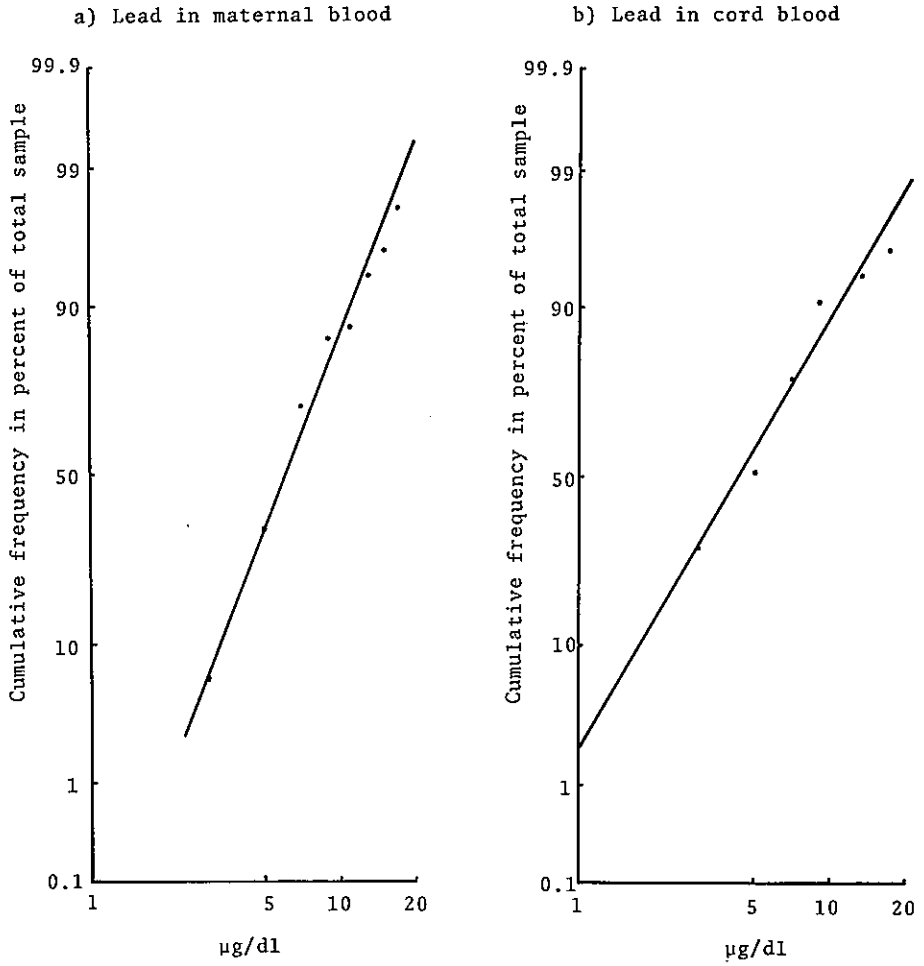


Fig. 2. Cumulative frequency plots of the data on concentrations of lead in maternal and cord blood

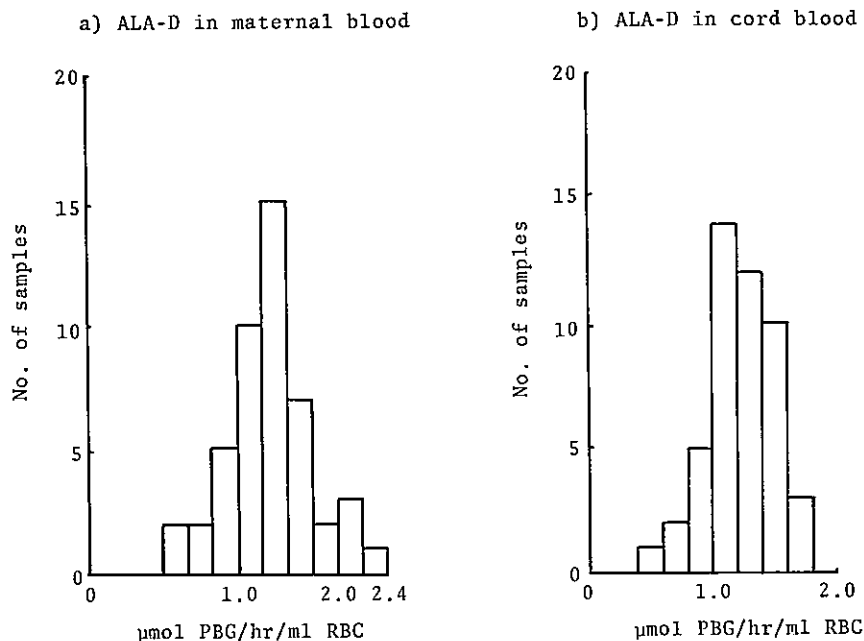


Fig. 3. Frequency distribution of  $\delta$ -aminolevulinic acid dehydratase (ALA-D) activities in maternal and cord blood

The relationship between Pb-B concentration found in maternal and cord blood is shown in Fig. 5. The figure shows that there was a close correlation between Pb-B in maternal and cord blood ( $r=0.85$ ,  $p < 0.01$ ).

The relationship between ALA-D activity in maternal and cord blood is illustrated in Fig. 6. The figure indicates that there was a good correlation between ALA-D activities in maternal and cord blood ( $r=0.58$ ,  $p < 0.01$ ).

The relationship between Pb-B and log ALA-D activity in maternal blood is illustrated in Fig. 7. The correlation coefficient was  $-0.29$  ( $p < 0.05$ ), and a certain correlation was observed between Pb-B and log ALA-D activity in maternal blood.

In Fig. 8 is shown the relationship between Pb-B and log ALA-D activity in cord blood. The correlation coefficient was  $-0.091$  and no significant correlation was observed between Pb-B and log ALA-D activity in cord blood.

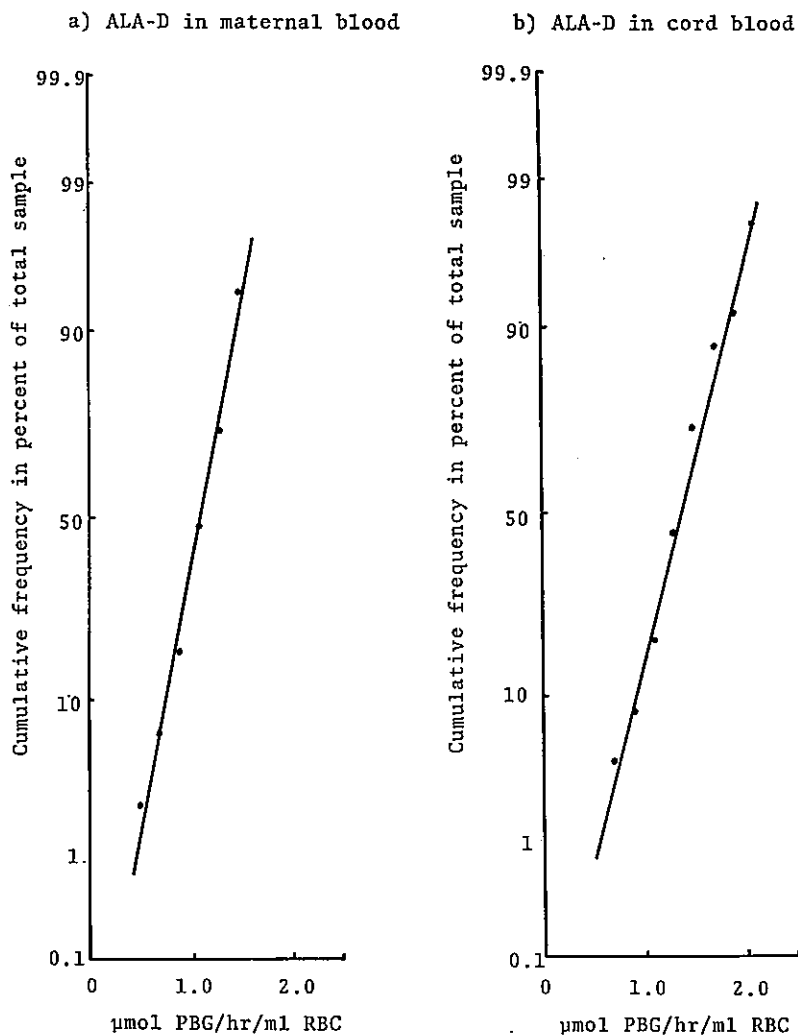


Fig. 4. Cumulative frequency plots of the data on  $\delta$ -aminolevulinic acid dehydratase (ALA-D) activities in maternal and cord blood

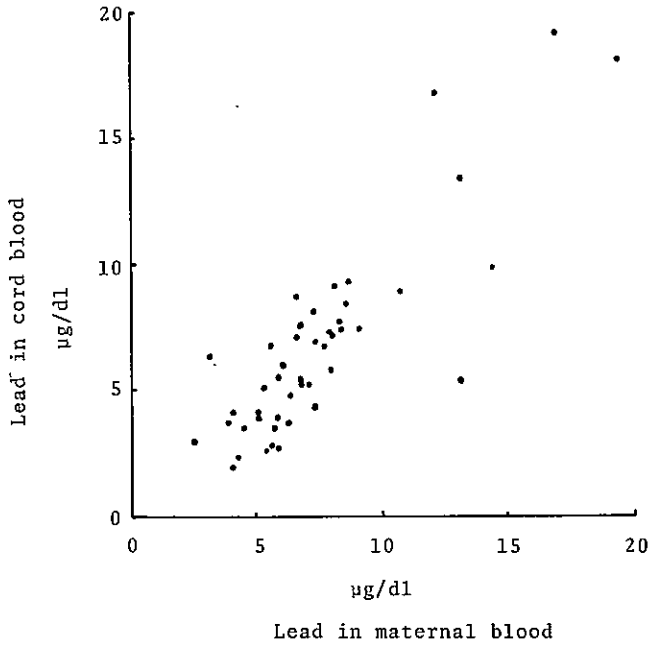


Fig. 5. Correlation between lead levels in maternal and cord blood

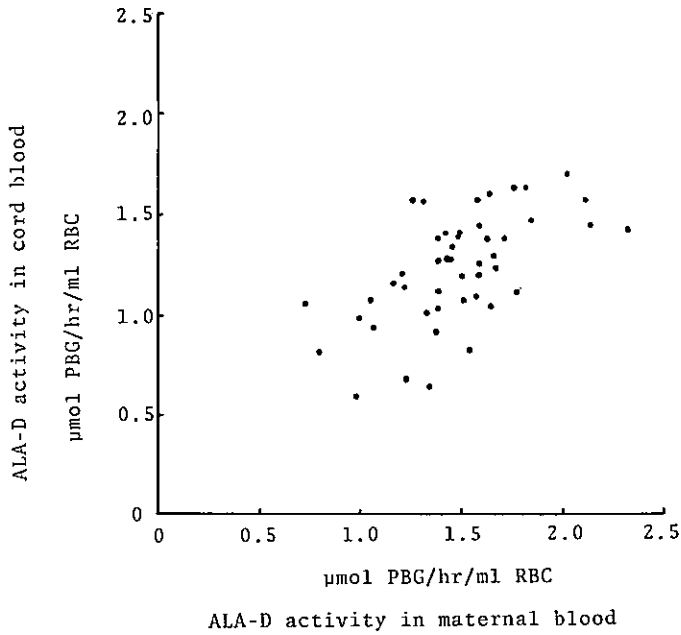


Fig. 6. Correlation between  $\delta$ -aminolevulinic acid dehydratase (ALA-D) activities in maternal and cord blood



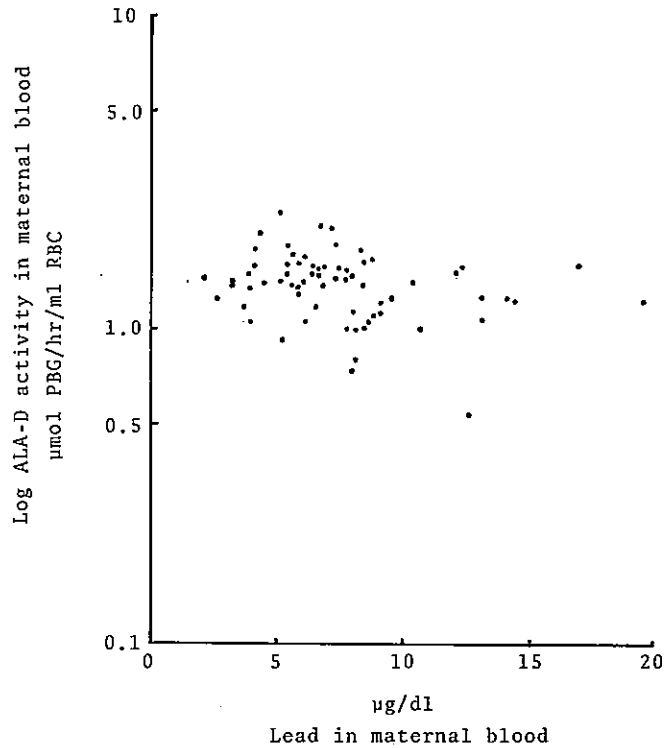


Fig. 7. Correlation between lead level and log  $\delta$ -aminolevulinic acid dehydratase (ALA-D) activity in maternal blood

#### DISCUSSION

The average Pb-B values for maternal and cord blood in our study were found to be slightly lower than those of any other studies in "normal" population of adult women<sup>11,14</sup>) or infants<sup>15,16,17,18</sup>). The differences between Pb-B levels in the present study and in other studies are assumed to reflect the degree of environmental lead exposure to pregnant mothers.

It has also shown in several epidemiological studies that cigarette smokers have slightly but consistently higher values of Pb-B than those of non-cigarette smokers<sup>19</sup>). In our study, however, none of cigarette smokers were included, and this would also be attributed to the lower values of Pb-B found in our study.

A close correlation was found between Pb-B levels in maternal and cord blood, similarly to the findings in other studies<sup>16,18,20</sup>). This finding suggests the

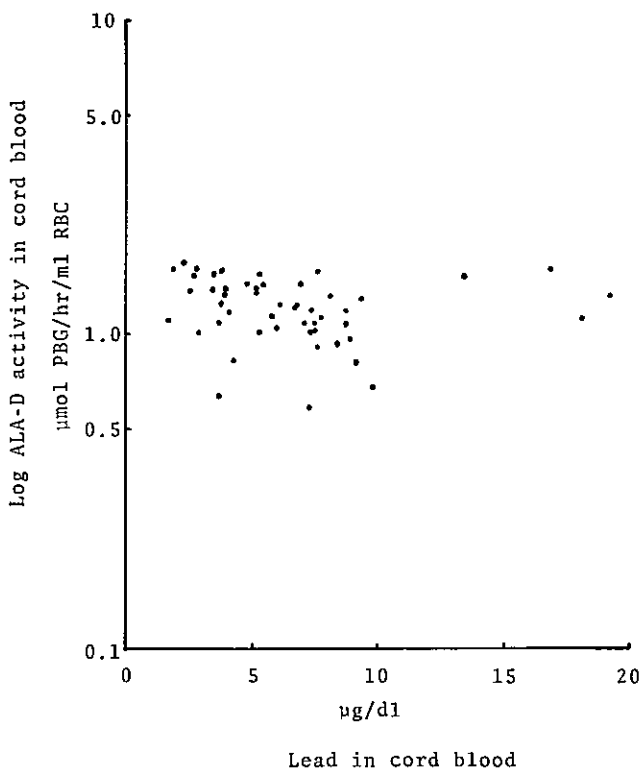


Fig. 8. Correlation between lead level and log  $\delta$ -aminolevulinic acid dehydratase (ALA-D) activity in cord blood

free passage of lead across the placenta from mother to fetus, which has been demonstrated in many animal species<sup>3,21)</sup> and humans<sup>4,5,6)</sup>.

A good correlation was found between ALA-D activities in maternal and cord blood in the present study. This finding would suggest the existence of genetic factors affecting the erythrocyte ALA-D activity, similar to the results reported by Wada *et al.*<sup>22)</sup>, although Maruta *et al.*<sup>33)</sup> could not find any relationship between ALA-D activities in maternal and cord blood.

A certain negative correlation was observable between Pb-B and log ALA-D activity in maternal blood, however, we could not confirm the existence of a demonstrable inverse relationship between these two parameters in cord blood.

The explanations for the latter observation is unknown, but Wada *et al.*<sup>22)</sup> concluded in their report that ALA-D activity in human blood was determined

by genetic and environmental factors as mentioned above, and was useful for the evaluation of lead exposure only when the Pb-B level was higher than a threshold value (around 15  $\mu\text{g}/\text{dl}$ ), although other authors cited different threshold values<sup>8,10,24,25</sup>. Our data revealed that most of the Pb-B values in maternal and cord blood were less than the threshold value<sup>21</sup>, and this would be one of the reasons for our observation, in which we could not confirm the existence of a significant inverse relationship between the Pb-B level and log ALA-D activity in cord blood.

Further studies into this problem seem to be necessary.

Part of this study was presented at the 36th Annual Meeting of the Japanese Society of Public Health in Kobe, Oct. 1977.

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