

Problem of Estimating Respiratory Lead Dose in Children

by John H. Knelson*

Children may be exposed to lead in their environment by a variety of mechanisms, but the final two common pathways involve ingestion and/or inhalation. The serious public health problem of overt lead intoxication from eating lead-based paint has tended to obscure low level toxicity which may be related to atmospheric lead pollution. No data exist which relate potential body burden or blood lead levels in children to ambient air lead levels. Extrapolation from respiratory lead uptake kinetics in adults is complicated by the differences in respiratory physiology, metabolism, and body compartment sizes existing between children and adults. These differences and models from pediatric pharmacology have been used to approach the problem of predicting respiratory lead dose in children from data based on adult uptake studies.

Introduction

The problem of estimating respiratory lead dose in children is a small aspect of the much more complex problem of assessing health hazards of aerosols in general. Complicated issues concerning particulate sampling, measurement of size and chemical composition, regional deposition and retention, distribution in body compartments, and relative toxicity of various species of inorganic lead particulates are very important but beyond the scope of this report. The two questions I wish to address here are: (1) what predictions can be made relating increase in blood lead concentrations to inorganic lead particulate concentrations in ambient air,

and (2) whether these predictions should be any different for children than adults.

Air Lead/Blood Lead Relationships in Adults

Three basic approaches have been used to estimate the relationship between ambient air lead levels, respiratory dose, and resultant lead concentrations in various body compartments, including circulating blood volume. Some of the first, and still some of the best data were acquired from controlled human exposures to air lead as well as dietary lead by Kehoe, Cholak, and their colleagues. These studies were conducted and reported over a number of years, but two of the most pertinent are those of Kehoe (1,2). More recently, extensive data from controlled laboratory exposure of animals as well as human subjects have been obtained by Coulston's group (3,4). The major difficulty

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with controlled environmental laboratory exposure studies is that particulate size and composition generated in the laboratory may not be the same as that occurring in ambient air (5). Epidemiologic observations of populations living in areas with differing air lead levels or studies of occupationally exposed individuals are a second valuable source of data (6,7). Data of this nature are often difficult to interpret because of problems in estimating the actual air lead levels to which the subject population is exposed as well as evaluating the contribution of dietary sources of lead. For these reasons, conflicting opinions of the relative importance of airborne lead exist (8-10). Finally, animal toxicology data have served to emphasize interspecies differences and the probable errors that result when animal uptake data are extrapolated to humans. Therefore, the controlled long term human volunteer studies provide the best available data base for calculating air lead/blood lead relationships for adult men.

The controlled uptake studies by Coulston et al. are still in progress, but a preliminary analysis of two exposure levels has been published (4). The results are summarized in Figure 1. Men exposed to average air lead levels of $10.9 \mu\text{g}/\text{m}^3$ and $3.2 \mu\text{g}/\text{m}^3$ for up to 20 weeks experienced significant elevation in blood lead levels. Men with the same diet

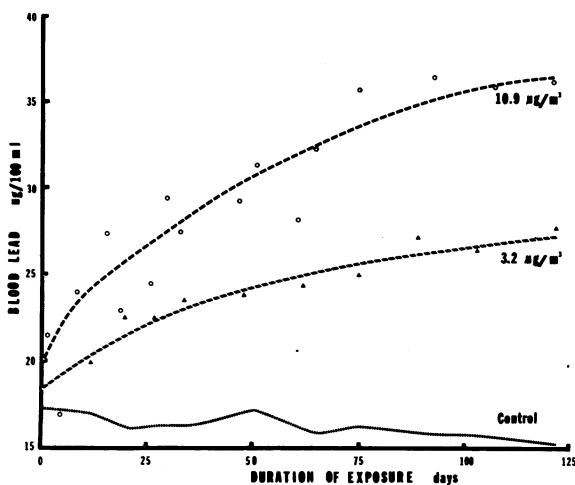


FIGURE 1. Respiratory lead exposure.

and activity schedules had no significant changes in blood lead. Blood lead concentrations of the exposed men returned to pre-exposure levels after the exposure ended.

Daily air lead determinations were used to calculate the respiratory dose of these relatively sedentary men assuming a daily ventilation of 15 m^3 , 37% retention of inhaled lead particulates, and 100% absorption of those retained. A model to describe the data was developed by using a transform of the independent variable (air lead) of the form $y = xM/(x + k)$, where M is the maximum or limit asymptotically approached by the dependent variable (blood lead) and k is the value of x when $y = M/2$ (Fig. 2). The value for M was established by taking the mean of the highest blood lead levels at the end of exposure; k is then defined as mean integrated respiratory dose at $M/2$. This model resulted in correlation coefficients between measured blood lead and air lead of better than 0.9 for both levels of exposure. Increases in blood lead concentrations based on this model were calculated for representative exposures and two arbitrary levels of ventilation (Table 1).

Relationship between Respiratory Dose Calculations in Children and Adults

Physiologic and metabolic differences between growing children and adults have not

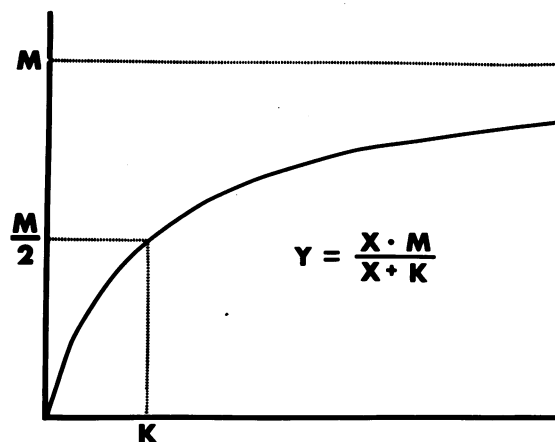


FIGURE 2. Blood lead concentration as a function of air lead.

Table 1. Predicted increase in blood lead concentrations.

Pulmonary ventilation, m ³ /day	Air lead, μg/m ³	Blood lead concentrations after various exposure times, mg/100 ml				
		20 days	40 days	60 days	80 days	100 days
15	1	1.9	2.4	2.7	2.9	3.1
15	2	2.1	2.9	3.4	3.7	4.0
15	3	2.5	3.5	4.2	4.6	5.0
20	1	2.1	2.6	2.9	3.1	3.3
20	2	2.4	3.2	3.7	4.0	4.3
20	3	2.9	4.0	4.6	5.1	5.4

often been recognized in developing the health data basis for environmental standards. Barltrop (11) has recently drawn attention to the importance of such considerations and has outlined some aspects of the problems, as has King (12).

In calculating a respiratory dose of any material, the first problem is to determine the amount of air inhaled per unit time (V_I). In free-ranging individuals it is not possible to make such measurements directly, so one must make estimates based on the variables known to influence V_I . The most important of these is metabolic activity, which in turn is most frequently related to energy production (kilocalories per unit time) and oxygen consumption (V_{O_2}).

Most of the available information on metabolic activity as a function of age has been obtained from carefully controlled caloric balance studies and not from measurements of V_{O_2} directly. The relationship between energy production and V_{O_2} varies somewhat with dietary composition. But heat production per liter of oxygen consumed ranges only from 4.7 kcal/l for fat, to 4.8 kcal/l. for protein and 5.0 kcal/l. for carbohydrate, so that factor has been ignored in the following calculations. For a typical diet, therefore, the relationship (1) is used:

$$\text{Metabolic rate (kcal/t)} = 4.83 V_{O_2} \text{ (l./t)} \quad (1)$$

The relationship between basal metabolic rate and age has been well-studied and is discussed in any standard textbook of physiology. In general, basal metabolism declines

from 55 kcal/m²-hr at 1 year of age to about 30 at age 40 years for men. The absolute values are somewhat less for women. Total caloric production has been reported for subjects of different ages, but the data are not as extensive as one might wish. Because energy production as well as V_{O_2} are best related to body surface area, I have elected to calculate total V_{O_2} using the DuBois metabolism table (13), standard height/weight table for children (14), and eq. (2), also from DuBois (13):

$$\text{Body surface area (m}^2\text{)} = 0.202 W(\text{kg})^{0.425} H(\text{m})^{0.725} \quad (2)$$

Those calculations result in a statistical statement relating basal metabolic rate to age from which V_{O_2} can be calculated as described.

The final step in this sequence is calculation of V_I from V_{O_2} . Relationship between these variables changes with level of activity as presented in Table 2. Data presented in that table are based on an extensive study of physiologic and metabolic changes during rest and exhaustive exercise by Luft (15). The ratio V_I/V_{O_2} is seen to range from about 27 to 37, depending on degree and type of exercise. The same ratio at rest is between 20 and 25.

Relative V_I at rest from 1 to 17 years of

Table 2. Relationship between V_{O_2} and V_I .

Type of exercise	$V_I V_{O_2}$
Bicycle	
To V_{O_2} max	34.39
To 75% V_{O_2} max	28.50
Rowing (arm and leg)	
15 strokes/min	29.31
20 strokes/min	30.59
25 strokes/min	33.84
Arm exercise (standing)	
246 kpm/min	33.62
333 kpm/min	33.81
555 kpm/min	37.06
Leg exercise (supine)	
333 kpm/min	26.99
555 kpm/min	28.78
1031 kpm/min	32.88

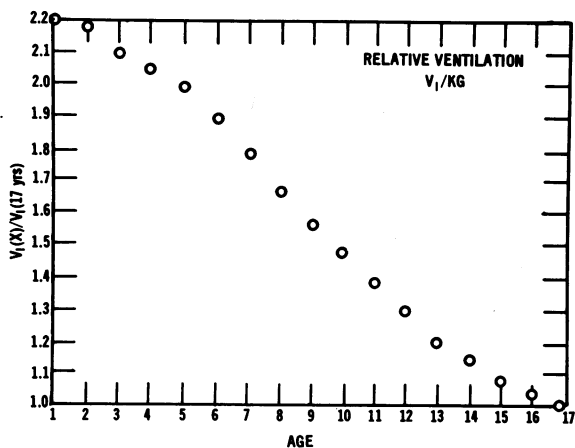


FIGURE 3. Relative ventilation as a function of age.

age has been plotted in Figure 3. The relationship between changing basic metabolic rate and changing surface area is beginning to come into equilibrium then, but more data are needed to define the relationship during the young adult years. Figure 3 therefore allows one to select an appropriate factor for predicting respiratory dose for children from data based on adult uptake studies. Relative ventilation as a function of age is not appreciably different for boys and girls, but absolute daily V_I at rest as shown in Figure 4 is slightly different because of difference in size and rates of maturation.

All the discussion to this point has dealt with ventilation and metabolic rates at rest.

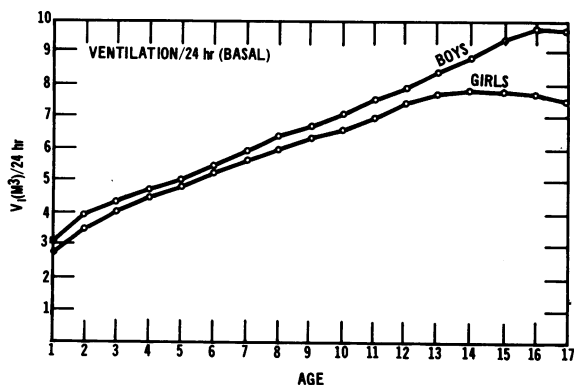


FIGURE 4. Daily ventilation as a function of age in boys and girls.

Children are known to have a higher resting metabolic rate and ventilation, and this has been described in some detail. It was also pointed out that the relationship between total ventilation and metabolism rises as level of activity rises. That relationship is roughly exponential, so increase in level of activity results in proportionally greater respiratory dose. A rather self-evident, but poorly quantified phenomenon is the greater activity levels generally maintained by children compared to adults. Thus children have a relatively greater ventilation at rest and also are probably more active than adults, resulting in a disproportionately large respiratory dose compared to either their mass or surface area.

Summary and Conclusions

Little consideration has been given to the special problems of estimating doses of potentially harmful substances children may be receiving via the respiratory tract. Virtually all available data on human respiratory toxicology is from adult studies. Some of the problems and an approach to calculating respiratory doses for children have been presented. With respect to exposure to airborne lead, as a specific example of a more general problem, comparison of Table 1 and Figure 3 allows one to estimate the change in blood lead concentration as a function not only of exposure conditions but age of a child. The questions concerning distribution of the respiratory dose in various body compartments and different susceptibility as a function of age remain largely unanswered.

REFERENCES

1. Kehoe, R. A. Experimental studies on the inhalation of lead by human subjects. *Pure Appl. Chem.* 3: 129 (1961).
2. Kehoe, R. A. The metabolism of lead in man in health and disease. The Harben lectures, 1960. *J. Roy. Inst. Public Health Hyg.* 24: 1, 101, 129, 177 (1961).
3. Griffin, T. B., et al. A comparative study of inhalation of lead particulates in animals and man. Paper presented at 11th annual meeting, Society of Toxicology, Williamsburg, Va., March 1972.

4. Knelson, J. H., et al. Kinetics of respiratory lead uptake in humans. In: Proceedings International Symposium, Environmental Health Aspects of Lead, Commission of European Communities, Amsterdam, 1972, pp. 391-401.
5. Lawther, P. J., et al. More observations on airborne lead. In: Proceedings International Symposium, Environmental Health Aspects of Lead, Commission of European Communities, Amsterdam, 1972, pp. 373-389.
6. Goldsmith, J. R., and Hexter, A. C. Respiratory exposure to lead: epidemiological experimental dose-response relationships. *Science* 158: 132 (1967).
7. Mehani, S. Lead retention by the lungs of lead-exposed workers. *Ann. Occup. Hyg.* 9: 165 (1966).
8. Tepper, L. B., and Levin, L. S. A survey of air and population lead levels in selected American communities. Department of Environmental Health, College of Medicine, University of Cincinnati, Cincinnati, Ohio. Final Report (Contract PH-22-68-28) December 1972.
9. Hasselblad, V., and Nelson, W. C. Additional analyses of the "Seven City Lead Study". In-house technical report. Human Studies Laboratory, National Environmental Research Center, Research Triangle Park, N.C., March 1973.
10. Jones, R. D., Commins, B. T., and Cernik, A. A. Blood lead and carboxyhemoglobin levels in London taxi drivers. *Lancet*: 302 (August 12, 1972).
11. Barltrop, D. Sources and significance of environmental lead for children. In: Proceedings, International Symposium, Environmental Health Aspects of Lead. Commission of European Communities, Amsterdam, 1972, pp. 675-681.
12. King, B. G. Maximum daily intake of lead without excessive body lead-burden in children. *Amer. J. Dis. Child.* 122: 337 (1971).
13. DuBois, E. F. *Basal Metabolism in Health and Disease*, 3rd ed., Lea and Febiger, Philadelphia, 1936.
14. Watson, E. H., and Lowry, G. H. *Growth and Development of Children*, 4th ed., Year Book Publishers, Chicago, 1962.
15. Luft, V. C., et al. Metabolic, respiratory, and cardiological measurements during exercise and rest. Department of Physiology, Lovelace Foundation for Medical Education and Research, Albuquerque, New Mexico. NASA contract report 9-7009 (December 28, 1971) NTIS #N72-18059.