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SMOOTHING OF EXPOSURE VARIABILITY AT THE RECEPTOR: IMPLICATIONS FOR HEALTH STANDARDS

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INTRODUCTION

THE ASSESSMENT of occupational exposures generally requires measurement of toxicant levels in the air. It is often presumed that, by merely comparing these air concentrations with a relevant index of allowable exposure (an air concentration associated with a legal standard or an unofficial guide), one can reach a fairly unambiguous decision about the hazards posed to workers' health. The logic of the argument proceeds as follows: measurements reflect exposures which reflect doses; allowable levels reflect doses which the promulgating group (or country) considers 'acceptable' given a dose–response relationship; therefore, if measurements exceed the allowable level then exposures constitute an unacceptable hazard and *vice versa*. (For a discussion of the philosophical basis of allowable levels see, for example, HATCH, 1972; HENSCHLER, 1984; RAPPAPORT, 1984.)

However, the above argument fails to consider the important fact that toxicant levels vary considerably from instant to instant and, indeed, from day to day. This variability, and the lack of guidance currently available for dealing with it, actually make the assessment of occupational exposures anything but straightforward (RAPPAPORT, 1984). One can be at a loss to decide not only how many measurements to make and when and where to make them and the proper averaging time, but also how to compare the data with the allowable level. Must *all* measurements be below this limit and, if not, then how often may they exceed it, and for how long, and by how much?

It is widely recognized that the empirical processes which produce airborne

exposures are random in nature (e.g. ROACH, 1966, 1977; COENEN, 1976; RAPPAPORT *et al.*, 1981). This suggests that exposures arising from a particular industrial operation comprise a distribution over time, the mean and the variance (and possibly other parameters) of which could be used for assessment purposes. A strategy focusing upon the mean level, for example, would require the demonstration that each worker's true mean exposure is less than the allowable level. Since this approach does not constrain either the frequency or the magnitude of excursions above the allowable level (as long as the mean is in control), its use might be appropriate in certain situations involving long-term chronic exposures. A strategy focusing upon both the mean exposure and the variance, on the other hand, allows overall levels and large exposures to be dealt with simultaneously, although at the expense of greater complexity. This approach presents some intriguing possibilities for assessing exposures to acutely toxic agents, to those which produce both acute and chronic effects, and perhaps to chronic toxicants which are eliminated from the body rapidly.

By defining assessment in terms of the parameters of exposure distributions, one takes advantage of the significant body of knowledge employed in statistical quality control; indeed, numerous methods are available either for estimating the mean and the variance or for testing relevant hypotheses. The critical question, therefore, is related less to the mechanics of arriving at decisions than to identifying situations which can reasonably be framed as either a one-parameter (mean only) or a two-parameter problem (mean plus variance). The purpose of this paper is to explore the functional relationships between long-term exposure and the toxicant burden and thereby shed light upon situations when use of these two approaches might be appropriate.

EXPOSURE AND RESPONSE

The relationship between a lifetime of exposure to a given chemical and the likelihood of disease can be extremely complex. At least three transfer functions come into play in first relating exposure to burden (toxicokinetics), then burden to damage (toxicodynamics) and, finally, cumulative damage to the likelihood of clinical response (RAPPAPORT *et al.*, 1982). The processes connected by these transfer functions are in series, the output from one being the input for another, so that each in turn is a necessary determinant of the ultimate outcome. Thus, even though the human database may not allow the latter processes of damage and disease to be adequately characterized, as is often the case, it is still useful to examine the preceding, and more tractable, relationship between exposure and burden.

The term 'burden' refers here to the amount of toxicant which is present at the receptor at any particular time. The burden thus represents the accumulation of individual doses received during each work shift. The term 'receptor' may be defined either in the classical sense, as a biochemical species or mechanism that is interfered with in some way by the toxicant, or in a more practical sense, as a tissue or organ which is susceptible to damage by the toxicant. It is also appreciated that some inhaled toxicants are biotransformed to the toxic species upon metabolism.

Returning to the efficacy of the mean and variance of inhaled air concentrations as measures of allowable exposure, the above argument suggests a useful line of inquiry. If fluctuations of receptor levels around the mean toxicant burden are significantly

smoothed relative to fluctuations of exposures about the mean air concentration, then use of mean exposures as the sole assessment criterion may be justified. It should be possible to investigate this smoothing with toxicokinetic models and to test predictions by comparing fluctuations of workers' airborne exposures (environmental monitoring) with those of toxicant levels in the body (biological monitoring).

The application of toxicokinetic principles to uptake and elimination of airborne toxicants is certainly not new. Numerous investigators have explored the relationships between occupational exposures and, for example, the deposition, retention and clearance of inhaled particles (see, for example, the review by LIPPMANN *et al.*, 1980), the uptake and elimination of solvent vapours (e.g. FISHEROVA-BERGEROVA, 1983), the accumulation and elimination of heavy metals (e.g. Task Group, 1972) and the use of unusual work schedules (e.g. ROACH, 1977; HICKEY and REIST, 1977; MASON and DERSHIN, 1976). However, with the notable exception of a pair of papers by ROACH (1966; 1977), the generic problem of exposure variability upon toxicant levels in the body has been largely ignored.

Roach identified the smoothing effects which uptake and elimination can exert upon toxicant burden relative to fluctuations in air levels, and correlated this with smoothing from the associated processes of air measurement and ventilation. Since the latter are inherently short-term, he focused upon the toxicant burden over time scales of hours to days and, because allowable levels specified an averaging time of 8 h, he dealt with a continuous regimen of 8 h of exposure followed by 16 h of non-exposure. This paper continues in the same vein but extends the scope to long-term accumulation, which requires consideration of a weekly regimen. The analysis will employ a single-compartment model; multi-compartment models which describe dampening effects associated with more complex chemical disposition in the body will be described separately.

DAILY UPTAKE

A single-compartment model depicts the body (receptor) as a single homogeneous unit within which the toxicant is uniformly distributed at all times. This simple construct has been widely used in toxicology to describe chemical disposition in the body as a whole and, as will be demonstrated, can be used to study the behaviours of toxicants in individual compartments of more complex systems. If the toxicant is inhaled at a constant rate each day and eliminated from the receptor by a first-order process (e.g. first-order reaction, diffusion, filtration) then the differential equation describing the rate of change of the amount of toxicant at the receptor is:

$$dX/dt = CK - k_x X, \qquad X(0) = X_0, \tag{1}$$

where $X(t)$ is the amount (mg) of toxicant at the receptor at time t, $C(t)$ is the air concentration (mg m^{-3}), K is the uptake constant ($m^3\ h^{-1}$) equal to the respiratory ventilation rate ($m^3\ h^{-1}$) times the fraction of chemical retained (dimensionless and assumed to be constant), K_x is the elimination constant (h^{-1}) (elimination can also be described in terms of the half-time (h) $T = 0.693/k_x$), and X_0 is the initial amount at the receptor (mg). The quantity CK represents the dose of toxicant received per hour of exposure.

Assuming for the moment that the air concentration remains constant, then

integration of equation (1) gives the amount of toxicant at the receptor at any time t, as

$$X(t)=(CK/k_x)(1-e^{-k_x t})+X_0e^{-k_x t}. \quad (2)$$

The two terms in equation (2) represent, respectively, the dose received during the current exposure and the residual burden from all previous exposures. The relative magnitudes of the two terms depend upon the exposure/non-exposure regimen and the value of the elimination constant k_x.

If the duration of continuous exposure were unlimited, then as t increased the quantity $e^{-k_x t}$ would tend to zero and the receptor burden would approach the equilibrium value of CK/k_x (ROACH, 1966). However, because t is fixed at 8 h for most occupational exposures, only toxicants in which $T \leq 2.4$ h can produce burdens of at least 90% of CK/k_x; that is, $(1-e^{-8k_x}) \geq 0.90$ when $T \leq 2.4$ h. These substances, which include most acute toxicants, represent a special class in which the receptor burden results entirely from the magnitude of C over periods of less than one shift.

ACCUMULATION AT THE RECEPTOR

Since 8-h shifts are typical, it is useful to standardize equation (2) for exposures of this duration and to examine the discrete distribution of receptor burdens observed immediately after each shift. If $C_{(i,j)}$ represents the 8-h time-weighted-average air concentration on the ith day ($i=1, 2, \ldots, 5$) of the jth week of exposure, then the corresponding post-shift burden $X_{(i,j)}$ is given by,

$$X_{(i,j)}=(C_{(i,j)}K/k_x)(1-e^{-8k_x})+X_{(i-1,j)}e^{-24k_x} \quad (3)$$

for $i=2$, 3, 4 and 5, and

$$X_{(1,j)}=(C_{(1,j)}K/k_x)(1-e^{-8k_x})+X_{(5,j-1)}e^{-72k_x}. \quad (4)$$

The last term in equation (4) points to the 72 h which elapse between the end of the fifth shift of one week and the beginning of the first shift of the next week.

When the half time T is greater than about one work shift, the residual burden from previous shifts becomes significant, indicating that the toxicant accumulates at the receptor from day to day. This is illustrated in Fig. 1 for a cycle of five 8-h workdays per week, a mean exposure

$$\mu_c=(1/n)\sum_{j=1}^{k}\sum_{i=1}^{5}C_{(i,j)}$$

over k weeks (where $n=5k$) of 1 mg m^{-3}, and an uptake constant (K) of 1 m^3 h^{-1}. The upper part depicts the random input function $C_{(i,j)}$ (solid line) and its mean (dashed line) while the lower part shows the corresponding output function $X_{(i,j)}$ and its expected value $E(X_{(i,j)})$. The latter is defined by the expressions

$$E(X_{(i,j)})=(\mu_cK/k_x)(1-e^{-8k_x})+E(X_{(i-1,j)})e^{-24k_x} \quad (5)$$

for $i=2$, 3, 4 and 5, and

$$E(X_{(1,j)})=(\mu_cK/k_x)(1-e^{-8k_x})+E(X_{(5,j-1)})e^{-72k_x}. \quad (6)$$

Figure 1 shows how the burdens of substances with short half-times (e.g. $T=10$ h) primarily reflect the dose just received, while those of toxicants with long half-times

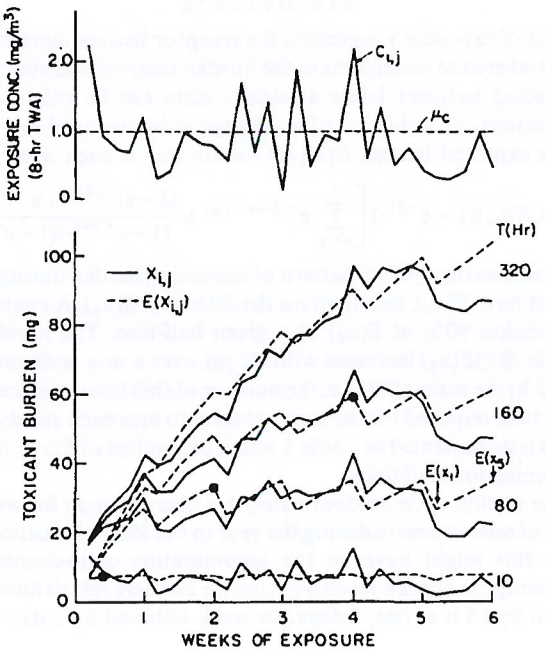

FIG. 1. Upper part: depicts 30 random 8-h exposures $C_{(i,j)}$ (solid line) and the mean exposure μ_c (dashed line). The lower part depicts the resulting 30 post-shift toxicant burdens $X_{(i,j)}$ (solid lines) and their expected values $E(X_{(i,j)})$ (dashed lines) for various elimination half-times T. (The uptake constant K is assumed to be 1 $m^3 h^{-1}$.) $E(x_1)$ and $E(x_5)$ are the expected values of the steady-state burdens on the first and fifth days of each week, respectively. Circles indicate the days when the post-shift burdens reach at least 90% of $E(x_5)$.

reach many times this amount. It is also apparent that the overall rate of accumulation over several weeks depends upon the mean exposure μ_c rather than the transient fluctuations from day to day.

When considering accumulation it is helpful to rearrange equations (5) and (6) to explicitly define the components of the burden,

$$E(X_{(i,j)}) = E(X_{(i,1)}) + E(X_{(5,1)})\left[\sum_{m=1}^{j-1} e^{-[168m-24(5-1)k_x}\right], \tag{7}$$

where

$$E(X_{(i,1)}) = (\mu_c K/k_x)(1-e^{-8k_x})\left[\sum_{n=1}^{i} e^{-24(n-1)k_x}\right],$$

and if $j=1$, then $E(X_{(5,1)})=0$.

Equation (7) shows that the toxicant burden is comprised of the daily dose plus the residual burden both from previous shifts in the current week and from previous weeks.

STEADY STATE

As the period of exposure progresses, the receptor burden increases until a steady state is achieved where the increments of the burden received and eliminated each week are equal. Expected toxicant levels at steady state can be calculated by repeated iteration of equations (5) and (6) until no change in burden is observed from week to week. Then, the expected burden $E(x_i)$ on the ith day of each week is,

$$E(x_i)=(\mu_c K/k_x)(1-e^{-8k_x})\left[\sum_{n=1}^{i} e^{-24(n-1)k_x}+\frac{(1-e)^{-120k_x})\ e^{-(48+24i)k_x}}{(1-e^{-24k_x})(1-e^{-168k_x})}\right]. \quad (8)$$

Figure 1 illustrates the cyclical pattern of increasing burden during each week from a low on the first day, $E(x_1)$, to a high on the fifth day, $E(x_5)$. A circle marks the shift when $E(X_{(i,j)})$ reaches 90% of $E(x_5)$ at a given half-time. The number of shifts (N) required to reach $(0.9)E(x_5)$ increases with T; yet over a very wide range of half-times ($20\ \text{h} \leq T \leq 3000\ \text{h}$) the ratio of $8N$, i.e. the number of shift hours worked, to T is close to unity. Thus, the time required for the toxicant level to approach steady state is about T shift hours. This is documented in Table 1 which lists values of $E(x_5)$, N and $8N/T$ over this range of elimination half-times.

Although the weekly cycle predominates, it is also common for workers to receive additional days of non-exposure during the year in the form of vacations and holidays. The effect that this might have on the accumulation of toxicants was tested by calculating the receptor burden resulting from an annual cycle defined as: 8 h of work per day followed by 16 h of rest, 5 days per week followed by 2 days (48 h) of rest, 4

TABLE 1. EXPECTED VALUES OF TOXICANT BURDEN AT STEADY STATE RESULTING FROM EXPOSURE TO MEAN AIR CONCENTRATION, $\mu_c = 1.0\ \text{mg m}^{-3}$, FOR 8 h/d, 5d/wk (The uptake constant, $K = 1.0\ \text{m}^3\ \text{h}^{-1}$)

Cycle*	T(h)	$E(x_5)$(mg)	N	$8N/T$
Weekly	0.25	0.36	<1	4.0
	1.0	1.44	<1	4.0
	5.0	5.01	1	1.6
	20	12.2	3	1.2
	80	34.7	10	1.0
	320	118	35	0.9
	1000	351	100	0.8
	3000	1038	900	0.8
Annual	80	34.7	10	1.0
	320	116	35	0.9
	1000	341	100	0.8
	3000	992	960	0.8

Legend: T is the elimination half time; $E(x_5)$ is the expected value of the post-shift burden on the fifth day of each week at steady state (weekly cycle) or the post-shift burden on the fifth day of the last week of the annual cycle; N is the number of days of exposure required for the post-shift burden to reach $(0.9)E(x_5)$.

* Weekly: continuous cycle of five 8-h days per week.

Annual: Twenty 8-h days per 29-day month, 12 months per 362-day year. Note: entries for $T < 80$ h are identical to those for weekly cycle.

weeks per month followed by an additional day of rest (29 days/mo), and 12 months per year followed by an additional 14 days of rest (362 days/yr; 240 working days/yr). Steady state in this case is the situation in which a repetitive pattern of burdens was observed over a period of a week or a month, depending upon the magnitude of T. The results, shown in Table 1, indicate that the additional 26 non-exposure days per year had a minimal effect on the accumulation of toxicants with $T \leq 3000$ h. Although the time required to reach steady state increased for the annual cycle (not shown), the steady-state level and the number of shifts (N) required to reach $(0.9)E(x_s)$ were essentially identical to the values observed for the continuous weekly cycle (Table 1). This indicates that the effect of additional days of non-exposure should be minimal, provided that the predominant cycle remains five 8-h exposures per week.

DISTRIBUTIONS OF RECEPTOR BURDENS

The above analysis indicates that a fixed distribution of random daily exposures $C_{(i,J)}$ with mean μ_c and variance,

$$\sigma^2_{c(8)} = (1/n) \sum_{J=1}^{k} \sum_{i=1}^{5} (C_{(i,J)} - \mu_c)^2, \text{ for } n = 5k$$

(over an 8-h averaging time), produces a series of post-shift receptor burdens. This series converges after about T hours of exposure to a stable pattern (*quasi* steady state) which varies about the mean burden μ_x. The variance of the process σ^2_x contains both a random component, associated with $\sigma^2_{c(8)}$, and a cyclical component, arising from the 72-h lag between work weeks.

Table 2 lists values of μ_x and the standard deviation of the receptor burden σ^2_x obtained by simulation (equations (3) and (4)) with 500 random values of $C_{(i,J)}$ derived from a lognormal distribution. Calculations of μ_x and σ^2_x employed the last $n = (500 - f)$ values of $X_{(i,J)}$, where f was based upon the half-time, so that steady-state conditions could be assumed. The parameters of the lognormal distribution were chosen such that $\mu_c = 1$ mg m^{-3} and the coefficient of variation, $CV_{c(8)} = \sigma_{c(8)}/\mu_c$, was between 0.2 and

TABLE 2. PARAMETERS OF DISTRIBUTIONS OF RECEPTOR BURDENS RESULTING FROM 500 RANDOM EXPOSURES $C_{(i,J)}$ DERIVED FROM A LOGNORMAL DISTRIBUTION WITH MEAN μ_c AND STANDARD DEVIATION $\sigma_{c(8)}$

$\mu_c \pm \sigma_{c(8)}$(mg m^{-3}) ($CV_{c(8)}$)	$\mu_x \pm \sigma_x$ (mg) (CV_x)					
	$T = 5$ h	10 h	30 h	100 h	300 h	1000 h
0.994 ± 0.237	4.94 ± 1.14	7.21 ± 1.49	14.8 ± 2.50	40.9 ± 3.90	116 ± 6.17	377 ± 14.3
(0.238)	(0.231)	(0.207)	(0.169)	(0.095)	(0.053)	(0.038)
0.984 ± 0.484	4.89 ± 2.34	7.14 ± 2.99	14.6 ± 4.31	40.5 ± 6.93	115 ± 11.6	374 ± 25.0
(0.493)	(0.478)	(0.420)	(0.294)	(0.171)	(0.101)	(0.067)
0.966 ± 1.05	4.80 ± 5.10	7.01 ± 6.53	14.4 ± 9.08	39.9 ± 14.3	113 ± 23.9	369 ± 49.1
(1.09)	(1.06)	(0.932)	(0.629)	(0.360)	(0.210)	(0.133)
0.966 ± 2.46	4.80 ± 11.9	7.03 ± 15.3	14.5 ± 21.4	40.3 ± 33.3	114 ± 53.3	370 ± 101
(2.55)	(2.48)	(2.18)	(1.47)	(0.826)	(0.465)	(0.272)
$n = 500$	495	495	490	485	450	375

Legend: μ_x and σ_x are the mean and the standard deviation of the post-shift toxicant burden at steady state based upon the last n values of $C_{(i,J)}$. $CV_{c(8)}$ and CV_x are the coefficients of variation of 8-h exposures and post-shift burdens, respectively.

2.5. This range of $CV_{c(8)}$ is equivalent to a range of geometric standard deviations ($\sigma_{g(8)}$ for 8 h averaging time) between 1.2 and 4.0; this range includes the great majority of estimates of $\sigma_{g(8)}$ associated with reports that occupational exposures were approximately lognormally distributed. (Note: $\sigma_{g(8)} = \exp[\sqrt{\ln(1+CV^2_{c(8)})}]$ (AITCHISON and BROWN, 1957.)

Table 2 shows that, for a given exposure distribution, both μ_x and σ_x increase with the half-time. Since the purpose here is to investigate fluctuations around the mean burden which at a given half-time may be large or small, it is useful to describe the relative fluctuations in terms of their coefficients of variation, where $CV_x = \sigma_x/\mu_x$. Table 2 lists values of CV_x associated with each distribution of burdens.

SMOOTHING AT THE RECEPTOR

It is clear from Table 2 that, for a given mean exposure, CV_x is directly proportional to $CV_{c(8)}$ and inversely proportional to T. The analysis is, therefore, simplified by defining a dimensionless dampening factor, $1/A = CV_x/CV_{c(8)}$, which is essentially a function of T alone. The quantity $1/A$ has the property of being close to unity when fluctuations in toxicant burden parallel those of daily exposure; it may be recalled this should happen when the half-time is less than about one work shift. When the half-time is longer than one shift, CV_x decreases relative to $CV_{c(8)}$ and $1/A$ decreases.

Figure 2 shows that for $0.2 \leq CV_{c(8)} \leq 2.5$, $1/A$ drops steadily from about 0.87 for $T = 10$ h to about 0.13 for $T = 1000$ h. The rate at which $1/A$ diminishes with increasing T is only marginally affected by exposure variability over this wide range of $CV_{c(8)}$. The bulge in the curve corresponding to $CV_{c(8)} = 0.2$ between $T = 10$ and 20 h indicates that, as the random component of σ_x^2 becomes small, the cyclic component (owing to elimination of toxicant) becomes proportionately larger (Fig. 1). The circles in Fig. 2 represent values of $1/A$ obtained from the useful approximation,

$$1/A \cong \frac{(1-e^{-24k_x})(1-e^{-168k_x})}{(1-e^{-120k_x})\sqrt{1-e^{-48k_x}}} \tag{9}$$

the derivation of which is given in the appendix.

It is possible to test the predicted smoothing effects by comparing relevant environmental (air) measurements with biological measurements of toxicant burden. The criteria for selecting data which might be used are straightforward, though numerous:

(1) air measurements should be performed by personal sampling and should cover the full shift;

(2) there should be sufficient numbers of measurements to reliably estimate day-to-day variability;

(3) measurements should be performed over several days for each worker (no pooling of workers), so that individual differences in uptake, elimination, and metabolism do not confound the analysis;

(4) biological measurements should relate directly to the toxicant burden, e.g. blood or tissue samples, rather than to the amount of toxicant eliminated (an exception involves toxicant in exhaled air which is in equilibrium with toxicant in the blood);

(5) biological samples should be collected at the end of the shift;

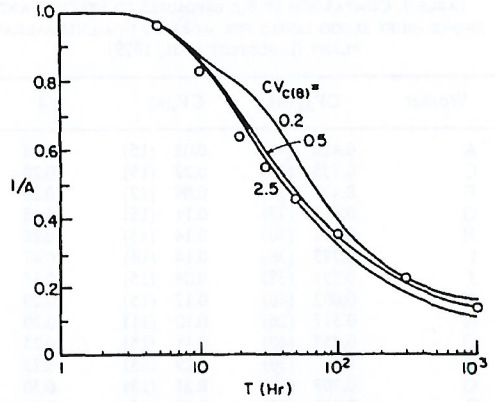

FIG. 2. The dampening factor $1/A = CV_x/CV_{c(8)}$ vs the elimination half-time T. Values of $1/A$ were obtained by simulation with equations (3) and (4) using 500 random, lognormally distributed values of $C_{(t,J)}$. CV_x and $CV_{c(8)}$ are the coefficients of variation of the post-shift toxicant burdens, and the 8-h TWA exposures, respectively. Circles show values of $1/A$ calculated with the approximation given in equation (9).

(6) workers should have been exposed for a sufficient period so that they may be presumed to be at steady state with the environment.

Although the above criteria are relatively easily satisfied with field studies designed to test the hypothesis, there are unfortunately very few relevant data which have been published in other contexts. The author has found only three published reports which satisfy these requirements. The first describes a study of 16 workers' exposure to mercury in a chloralkali plant where both full-shift exposures and blood were monitored frequently over 8 weeks (LINDSTEDT *et al.*, 1979). The investigators of that study generously allowed the author to inspect the original data. The results are summarized in Table 3. Values of $CV_{c(8)}$ and CV_x were obtained by adjusting the CVs derived from the data (CVD) for the precision of measurement. The CVs for air sampling and analysis and blood analysis are estimated to be 0.10 and 0.03, respectively. Thus, $CV_{c(8)} = \sqrt{CVD^2_{c(8)} - (0.10)^2}$, and $CV_x = \sqrt{CVD^2_x - (0.03)^2}$. The exposures of these workers exhibited a range of day-to-day fluctuations of $0.29 \leq CV_{c(8)} \leq 1.16$ with a mean ($\overline{CV_{c(8)}}$) of 0.62 while blood mercury levels fluctuated in the range of $0.08 \leq CV_x \leq 0.29$ with a mean ($\overline{CV_x}$) of 0.15.

The amount of smoothing expected for mercury in the blood requires information about the half time. CHERIAN *et al.* (1978) measured the elimination of radioactive mercury from the red blood cells and plasma of five human volunteers who had received a single dose by inhalation of the vapour; the mean half-time was 74 h for the red blood cells and 85 h for the plasma. Using a value of 80 h for whole blood, the expected value of $1/A$ is 0.38 for $\overline{CV_{c(8)}} = 0.62$ (Fig. 2). The observed values of $0.15 \leq 1/A \leq 0.47$ with a mean of 0.25, therefore, suggest marginally greater than expected smoothing. (Note: mercury is distributed from the blood to the receptors, the kidney and the brain, where the half-times are much longer than for the blood.)

The other two published studies which yielded usable data involved industrial exposures to inorganic lead. Both investigations compared individual workers' 8-h

TABLE 3. COMPARISON OF 8-h EXPOSURES TO MERCURY AND END-OF-SHIFT BLOOD LEVELS FOR WORKERS IN A CHLORALKALI PLANT (LINDSTEDT *et al.*, 1979)

Worker	$CV_{c(8)}(n)$	$CV_x(n)$	$1/A$
A	0.420 (40)	0.08 (15)	0.18
C	0.755 (40)	0.22 (15)	0.28
F	0.447 (30)	0.09 (12)	0.20
G	0.614 (39)	0.11 (15)	0.18
H	0.514 (40)	0.14 (15)	0.28
I	0.293 (38)	0.14 (14)	0.47
J	0.551 (38)	0.08 (15)	0.15
K	0.602 (40)	0.12 (15)	0.20
N	0.517 (26)	0.10 (11)	0.20
O	0.457 (40)	0.11 (15)	0.25
P	1.16 (38)	0.29 (15)	0.25
Q	0.709 (40)	0.21 (15)	0.30
R	0.684 (40)	0.18 (15)	0.26
S	0.829 (34)	0.24 (13)	0.30
T	0.903 (39)	0.22 (14)	0.24
U	0.457 (30)	0.13 (12)	0.28
Mean	0.620	0.15	0.25

Legend: $CV_{c(8)}$ is the coefficient of variation of 8-h exposures adjusted for a measurement error of 0.10; CV_x is the coefficient of variation of post-shift toxicant burden adjusted for a measurement error of 0.03; n is the number of measurements; $1/A$ is $CV_x/CV_{c(8)}$.

airborne exposures to inorganic lead dust or fume with end-of-shift blood values. The first described exposures of five workers in an alkyllead manufacturing plant over a 6-week period (COPE *et al.*, 1979).

The data, which have been adjusted for measurement errors of 0.10 for air sampling and analysis and 0.08 for blood analysis, are summarized in Table 4. The variability of daily exposures ranged from $0.52 \leq CV_{c(8)} \leq 0.74$ with $\bar{C}\bar{V}_{c(8)} = 0.63$ and of blood lead, $0 \leq CV_x \leq 0.08$ with $\bar{C}\bar{V}_x = 0.04$. The values of $1/A$ ranged from $0 \leq 1/A \leq 0.11$ with a mean of 0.06. The second study investigated lead exposures in three factories of different types (acid-battery manufacture, pigment manufacture and a zinc and lead smelter) over 12 weeks. Only the means of the individual workers' CVs were reported; these are given in Table 4 after adjustment for measurement errors as above. Values of $\bar{C}\bar{V}_{c(8)}$ were 0.72, 0.68 and 0.57 for the three factories, while values of $\bar{C}\bar{V}_x$ were 0.04, 0.08 and 0.06. Taking the ratios of the mean CVs gives values of $1/A$ of 0.05, 0.11 and 0.10, which are similar to those obtained from the data of COPE *et al.* (1979).

MARCUS (1979) estimated the half-time of lead in the blood, on the basis of a three-compartment composite model, to be 820 h (34.4 *d*). This half-time suggests that $1/A$ should be between 12 and 14% (Fig. 3) compared with an observed range for the four groups of workers of between 0.05 and 0.11.

These limited published data offer tantalizing evidence that the predicted smoothing effects are, in fact, very close to those which actually accompany occupational exposures. It is hoped that the future will provide much more data over wide ranges of T and $CV_{c(8)}$ to test the hypothesis more conclusively.

TABLE 4. COMPARISON OF 8-h EXPOSURES TO INORGANIC LEAD AND END-OF-SHIFT BLOOD LEVELS FOR WORKERS IN AN ALKYLLEAD MANUFACTURING PLANT (COPE *et al.*, 1979)

Worker	$CV_{c(8)}(n)$	$CV_x(n)$	$1/A$
A	0.57 (36)	0.06 (7)	0.11
B	0.74 (23)	0.02 (5)	0.03
C	0.60 (34)	0.04 (7)	0.07
D	0.71 (36)	0.08 (7)	0.11
E	0.52 (33)	0 (7)	0
Mean	0.63	0.04	0.06

Legend: Same as Table 3 except that CV_x was adjusted for a measurement error of 0.08.

TABLE 5. COMPARISON OF 8-h EXPOSURES TO INORGANIC LEAD AND END-OF-SHIFT BLOOD LEVELS FOR WORKERS IN THREE FACTORIES (KING *et al.*, 1979)

Factory	No. workers	$\bar{C}V_{c(8)}$	$\bar{C}V_x$	$1/A$
Battery	19	0.72	0.04	0.05
Pigment	34	0.68	0.08	0.11
Smelter	48	0.57	0.06	0.10

Legend: $\bar{C}V_{c(8)}$ is the mean of all individual workers' $CV_{c(8)}$ values (adjusted for a measurement error of 0.10) based upon 10 measurements per worker; $\bar{C}V_x$ is the mean of all individual workers' CV_x values (adjusted for a measurement error of 0.08) based upon at least three measurements per worker; $1/A$ is equal to $\bar{C}V_x/\bar{C}V_{c(8)}$.

CONCLUSIONS