

A SPECULATION ON THE IMPORTANCE OF CONCENTRATION FLUCTUATIONS IN THE ESTIMATION OF TOXIC RESPONSE TO IRRITANT GASES

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(Received April 25, 1984; accepted May 17, 1984)

Several authors at this symposium have drawn attention to the importance of concentration fluctuations in assessing the reliability of hazard range estimates for combustible materials, emphasising that the “instantaneous” concentration may well fall within the upper and lower flammable limits even though the time-averaged value is outside those limits. There would appear to be an analogous effect applying to certain toxic materials such as ammonia and chlorine, for which there is evidence that there is a weighting on concentration in determining the toxic response for exposure by inhalation. This is usually expressed in the form of the probit relationship, which expresses the varying susceptibility among individuals in a population,

$$Pr = a + b \ln(c^n t) \quad (1)$$

where the weighting on concentration, c , appears in the index n . The duration of exposure is t , and the coefficients a and b express the positions of families of mortality levels (LD_{05} , LD_{50} , LD_{95} etc.) on a graph of c vs. t . The probit relationship may be applied to various circumstances in which a population (not necessarily human) may be expected to show varying susceptibility to some stressing agent, and was largely developed in the context of tests on the effectiveness of insecticides, as described by Finney [1].

The probit Pr is a normally distributed variable with a mean of 5 and a standard deviation of 1, so that for a population exposed to certain combinations of c and t the percentage mortality is 50% for $Pr = 5$, $\approx 16\%$ for $Pr = 4$, $\approx 98\%$ for $Pr = 7$, and so forth. The values of the index n and the coefficients a and b utilised by different authors for ammonia and chlorine vary widely, as reviewed by Griffiths and Megson [2] who explore the implications of this wide variation in terms of predicted hazard ranges for notional releases of those materials. However, for these two substances the index n as given in the references reviewed in [2] is either 2 or 2.75. For some substances there appears to be no weighting on c in the toxic response, in which case $n = 1$ and the substance conforms to

what is known as Haber's Law, i.e. one can, within some limits, linearly trade-off concentration and duration without altering the percentage mortality.

Griffiths and Megson suggest that a crude estimate of the importance of concentration fluctuations for toxic response may be obtained by considering two equal dosages (dosage being $\int_0^{t_s} c(t)dt$, where t_s is the sampling or exposure time), the one being composed of a steady concentration \bar{c} for time t_s , and the other being composed of a series of peaks of concentration c_p experienced for a total time t_p , interspersed with zero concentration for total time t_0 , where $t_p + t_0 = t_s$. This situation is depicted schematically in Fig. 1. Defining the intermittency of the exposure, I , as the fraction of t_s during which the concentration is zero (following the definition of Murliss and Jones, [3]),

$$I = (t_s - t_p)/t_s \quad (2)$$

and setting the dosages equal

$$\bar{c}t_s = c_p t_p \quad (3)$$

we have

$$t_p = t_s(1-I) \quad (4)$$

and

$$c_p = \bar{c}/(1-I) \quad (5)$$

Substituting from (4) and (5) in eqn. (1), the probit variable $c^n t$ becomes $c_p^n t_p$, so that

$$Pr = a + b \ln \left\{ \left(\frac{1}{1-I} \right)^{n-1} \bar{c}^n t_s \right\} \quad (6)$$

This implies that the probit, and therefore the percentage mortality, becomes larger as the exposure becomes more intermittent, for a given dosage. The behaviour of this function is depicted in Fig. 2, which makes use of the chlorine probit relationship advanced by Eisenberg et al. [4], for which $a = -17.1$, $b = 1.69$ and $n = 2.75$. It should be stressed that this is only one of several such relationships to be found in the literature. Harper [5], from whom Fig. 2 is taken, has plotted the behaviour for this and other probits, which yield similar patterns. Clearly the enhanced toxic response cannot increase without limit, since, as pointed out by Ride [6] the characteristics of the receptor, the lung in this case, will impose some physical averaging time on the fluctuations in concentration. However,

Fig. 2. Showing the enhancement of percentage mortality with increased intermittency using the modified probit relation (equation (6)) and the coefficients for chlorine given by Eisenberg et al. [4]. The values of the percentage mortality at $I = 0$ chosen for illustration are 0.1, 5, 10, 20, 50, 80 and 90%.

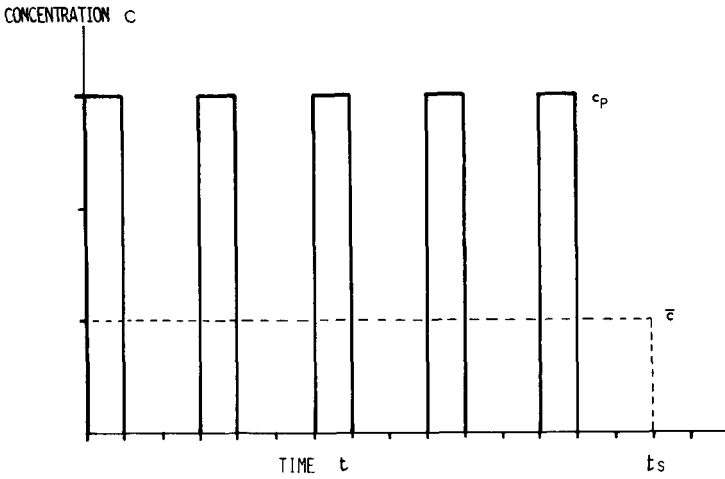
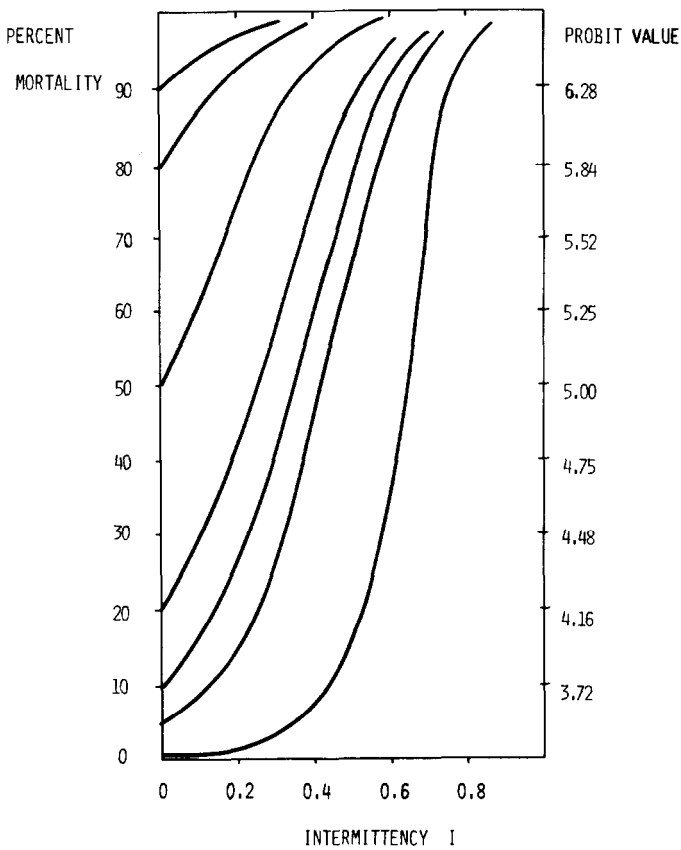


Fig. 1. Schematic representation of two exposures involving equal dosage: dashed line: \bar{c} for t_s ; solid line: c_p for total but intermittent time t_p ; total time with zero concentration is t_0 ; and $t_s = t_0 + t_p$.



Ride concludes, from similar considerations but based on fluctuation data rather than the artificial scheme used here, that there will be a significant effect. The general conclusion is that concentration fluctuations may well yield a significant enhancement in percentage mortality resulting from exposure to some toxic irritant gases, and this places an additional premium on the value of such data obtained from field tests such as those reported at this meeting. Further examination of the significance of this effect is called for.

Acknowledgements

During the period when this work was undertaken Mr. A.S. Harper was supported by an Advanced Course Studentship from the Joint Committee of the SERC/SSRC.

References

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