evaluated. In this example some of the concentrations could be zero to cope with a break in exposure, c_2 or $c_3 = 0$, or with retirement, $c_4 = 0$. Then the cumulative dose is given by:

$$\text{cumulative dose} = c_1 t_1 + c_2(t_2 - t_1) + c_3(t_3 - t_2) + c_4(t_4 - t_3)$$

This is how the cumulative dose would be evaluated in practice, but to simplify a more general approach it may also be written as an integral. Suppose exposure started at time zero and is to be evaluated up to time t, and that the concentration at time u is $c(u)$ for $0 \leqslant u \leqslant t$; again $c(u)$ would be zero during breaks in exposure or after retirement. Then

$$\text{cumulative dose} = \int_0^t c(u)\,\mathrm{d}u$$

This measure attaches no more importance to exposure a long time ago than to recent exposure, and does not alter after exposure has ended. Both of these properties are unrealistic for a disease, such as asbestosis, which is dependent more on early exposure than on recent exposure and which may develop after exposure has ended. The simplest way of allowing for both of these points was given by Jahr (1974) who suggested that each component of exposure should be weighted by the time which has elapsed since the exposure occurred. Thus, cumulative dose weighted by time since exposure is given by

$$\int_0^t (t-u)\,c(u)\,\mathrm{d}u$$

and, in practice, evaluated by summing contributions of the form

$$c_2(t_2 - t_1)\,\{t - \tfrac{1}{2}(t_1 + t_2)\}$$

over each period of exposure to a fixed concentration.

The weighting factor could be regarded as the time that the dust has been in the lungs if elimination has not taken place. Looking at the measure in this way, and postulating that elimination does occur, leads to a generalisation.

Suppose that, over the long term, dust is eliminated from the lungs at a rate proportional to the amount in the lungs, and the constant of proportionality is λ; in other words, in the absence of further exposure the amount of dust in the lungs declines exponentially at rate λ and will be reduced to one half of its level in time $T = \ln 2/\lambda$, the half-life time. The actual amount of dust deposited in the lungs is unknown, but is assumed to be proportional to the concentration. Then the amount of dust in the lungs at time v is, apart from a constant of proportionality, $A(v)$ given by:

$$A(v) = \int_0^v c(u)\,\mathrm{e}^{-\lambda(v-u)}\,\mathrm{d}u$$

If it is supposed that each component of dust which was deposited in the lungs contributes to the dose for the time it remains in the lungs then the dose $D(t)$ evaluated at time t is given by:

$$\begin{aligned} D(t) &= \int_0^t A(v)\,\mathrm{d}v \\ &= \int_0^t \int_0^v c(u)\,\mathrm{e}^{-\lambda(v-u)}\,\mathrm{d}u\,\mathrm{d}v \\ &= \int_0^t c(u) \int_u^t \mathrm{e}^{-\lambda(v-u)}\,\mathrm{d}v\,\mathrm{d}u \\ &= \frac{1}{\lambda}\int_0^t c(u)\,\{1 - \mathrm{e}^{-\lambda(t-u)}\}\,\mathrm{d}u \end{aligned}$$

This is the generalised measure which, except for infinite λ, has the properties that, first, it gives more weight to exposure a long time ago than to recent exposure and, second, it continues to increase after exposure has ended. If λ tends to infinity then D tends to zero, but in such a way that λD tends to cumulative dose. Thus, in effect the cumulative dose may be considered as a special case of the generalised dose when elimination of dust from the lungs takes place very quickly. If λ tends to zero, then D tends to the cumulative dose weighted by time since exposure which, therefore, is also a special case of the generalised measure when there is no elimination of dust from the lungs.

To summarise, the generalised measure consists of a family of dose measures with each member of the family defined by the parameter λ, or, in an equivalent manner, by the half-life time T. The full family is obtained by allowing T to vary from zero to infinity. The approach followed here is akin to that of the British Thoracic and Tuberculosis Association (1975).

DOSE-RESPONSE RELATIONSHIPS

If P is the prevalence of a sign at dose D, then a dose-response relationship is defined by a functional relationship between P and D, that is, $P = f(D)$. All the relationships considered are such that P is zero when D is zero, and as D increases above zero then so also does P; this excludes relationship