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THE ASSESSMENT OF MAJOR HAZARDS: THE LETHAL TOXICITY OF CHLORINE

PART 2, MODEL OF TOXICITY TO MAN

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Summary

The information available on the lethal toxicity of chlorine to animals and man has been reviewed in a previous paper. In the present paper this information is used to derive a revised estimate for the lethal toxicity to man. A distinction is made between less vulnerable and more vulnerable populations and between different levels of physical activity, with a standard level defined which is applicable to most daytime activity. Mortality is expressed in terms of a lethal toxic load which is a function of concentration and time. The concentrations lethal at the 50% level for a 10 min exposure with standard level of activity are estimated as 433, 173 and 364 ppm for the regular, vulnerable and average population, respectively, and those for a 30 min exposure as 250, 100 and 210, respectively. The probit equation derived for the regular population at the standard level of activity is

$$Y = -8.29 + 0.92 \ln L^*$$

with

$$L^* = \Sigma C^2 T$$

where C is concentration (ppm), L^* toxic load (ppm^2 min), T time (min) and Y the probit. A methodology for the application of the toxicity relationships in hazard assessment is given.

Introduction

In a previous, complementary paper [1] the information available on the toxicity of chlorine to animals and to man was reviewed with the aim of deriving a model for its lethal toxicity to man which is as soundly based as the data allow. The estimate sought is a realistic rather than a conservative one. It is considered that in the assessment itself the values used should be the most probable ones. The results of the assessment, which should then be tested for sensitivity, may be evaluated using any degree of conservatism

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which is thought to be appropriate. It was suggested that with some qualification the work of Underhill [2] provides a basis for estimating the lethal toxicity of chlorine to man, but that in practical situations it is necessary to allow for the various factors which influence man's response.

The present paper reviews the effects of physical activity and in particular of inhalation rate, the effectiveness of medical treatment and the form of the lethal toxic load function and presents a model for the lethal toxicity of chlorine to man and a methodology for its use in hazard assessment.

Physical activity

It is to be expected that man will not simply remain passive in the face of a toxic threat but will react by some form of physical activity such as seeking to escape or to obtain shelter.

There are two main effects of such activity. The first is that larger volumes of the contaminated air are inhaled. Some data on inhalation rates given by Henderson and Haggard [3] are shown in Table 1. It is clear from these data that the inhalation rate is greatly increased by activity relative to resting as a base case, and that the factor for enhanced activity can be as high as 15. The injury suffered as a result of more rapid inhalation may be increased, but it is not obvious how this should be allowed for. This is discussed further below.

The other effect of enhanced activity is that larger amounts of oxygen are required by the body. Table 1 gives data on this aspect also. This increased oxygen demand may occur during exposure and/or after exposure. In principle, further factors might be defined to take these aspects into account. It is proposed in the absence of further information not to make specific allowance for these factors here, but it is important to bear them in mind as ones which may be relevant in certain situations.

TABLE 1

Inhalation and oxygen consumption rate for various levels of enhanced activity for man (after Henderson and Haggard [3])

Activity	Inhalation rate (l/min)[a]	Oxygen consumption rate (l/min)[b]
Rest in bed, fasting	6	0.240
Sitting	7	0.300
Standing	8[c]	0.360
Walking, 2 mile/h	14	0.650
Walking, 4 mile/h	26	1.200
Slow run	43	2.000
Maximum exertion	65—100	3.000—4.000

[a] Measured at 0°C and 760 mmHg.
[b] Measured at 20°C.
[c] This value is quoted by Meyer [4] and by Prentiss [5] also.

In fact there is a strong possibility that the relatively high proportion of acute deaths experienced in the gas attacks described may well be due to increased oxygen demand during exposure. If so, the use of the gas warfare data to estimate the proportion of acute deaths will take increased oxygen demand during exposure into account. As far as increased oxygen demand after exposure is concerned, this appears to be of much less importance for chlorine than for phosgene.

Inhalation rate

The effect of inhalation rate on the injury caused by a given concentration of chlorine in air is not obvious, but it is important, because it is quite conceivable that high inhalation rates will increase the injury severalfold. It is necessary, therefore, to attempt to make some estimate of the effect of inhalation rate. The basic assumption made is that over a given inhalation period injury is a function of the mass of chlorine absorbed.

The rate of absorption of chlorine in the lung is a mass transfer process and this process may be modelled. Descriptions of the respiratory system, including quantitative data, are given in standard physiology texts such as Mountcastle [6]. The amount absorbed is the product of the alveolar ventilation rate and the difference in the inhaled and exhaled chlorine concentrations. It is also equal to the product of the pulmonary diffusion capacity and the difference between the actual and equilibrium partial pressure of chlorine at the alveolar membrane wall. Finally, it is also equal to the sum of the amount of chlorine transported out of the lung capillaries by the blood and of that reacted in the alveolar tissue.

The lung is a highly effective mechanism for mass transfer. At rest the degree of saturation with oxygen of the blood in the lung capillaries is high and the equilibrium partial pressure of oxygen in the blood is also high. The amount of oxygen transferred into the blood is the product of the pulmonary diffusion capacity, which is large, and the oxygen partial pressure difference, which is small. When exercise occurs, the amount of oxygen required is much greater and it is obtained by a more rapid circulation of blood through the lung, which reduces the concentration of oxygen in the blood in the lung capillaries and thus opens up a much greater oxygen partial pressure driving force. The pulmonary diffusion capacity has been studied and values estimated for O_2, CO_2 and CO. It is proportional to the solubility of the gas and inversely proportional to the square root of its molecular weight.

Another important aspect is the solubility of the gas. For chlorine the situation is complicated by the hydrolysis of chlorine to hypochlorous acid. The solubility of chlorine and its hydrolysis have been extensively studied and data are available on the solubility of unhydrolysed chlorine and on the equilibrium and rate constants for the hydrolysis [7—10]. No data have been found for the solubility of chlorine in blood plasma, but the solubility of

other gases such as O_2, CO_2 and N_2 is approximately 10% less than in water.

If it is assumed that the chlorine is simply physically absorbed into the blood, there will be a gradual accumulation of chlorine in the blood which will exert a corresponding equilibrium partial pressure at the alveolar membrane so that the concentration of chlorine in the blood will rise exponentially to an equilibrium value and absorption will tail off. However, this model does not appear to be consistent with the information available on the damage done to the body by chlorine. The evidence indicates that the damage is essentially confined to the lung.

A more appropriate assumption appears to be that the lung is a sink for the chlorine, which reacts with the alveolar tissue. This means that the venous blood entering the lung capillaries will contain very little chlorine. The maximum concentration of chlorine in the blood leaving the lung may then be obtained by solving the mass balance. Simple calculations based on the physiological parameters and the solubility of unhydrolysed chlorine indicate that for a man at rest the concentration of exhaled chlorine will be less than half of the inhaled concentration. The actual value will be less than this maximum, since the concentration of chlorine in the blood will be reduced both by hydrolysis and by reaction with the tissues. Thus even at rest almost all the chlorine inhaled will be absorbed. This will also be true for moderate increases in physical activity, since the increase in inhalation rate is accompanied by an increase in the circulation of the blood through the lungs.

Further support for this interpretation is afforded by experiments by Lehmann [11] in which he measured the inlet and outlet concentrations of chlorine in chlorine-contaminated air breathed by men. The inlet concentration of chlorine was 2 ppm, the outlet concentration undetectable, the absorption being thus total. This evidence is not conclusive, since the chlorine concentration is low, but it points in the right direction.

It is proposed, therefore, that as a first approximation the effect of inhalation rate be taken into account by defining a factor ψ_1 which is applied directly to the concentration to correct for inhalation rate.

Medical treatment

Appropriate medical treatment may effect a reduction in the mortality from exposure to chlorine. It is likely to be much more effective in preventing delayed deaths than acute deaths. It is proposed that this be allowed for by defining a medical treatment factor ψ_2 which is applied to the proportion of delayed deaths, or rather in this context potential delayed deaths, to yield a proportion of recoveries.

Concentrations intolerable to man

Information is available on the effect on man of concentrations of chlorine which are not normally lethal. Some data on concentrations which

are tolerable and intolerable to man were given in Table 12 of Ref. [1]. At concentrations of about 4 ppm irritation is said to be experienced and normal work to be impossible. Dangerous concentrations are variously given as 14—21 and 40—60 ppm for 1/2—1 h, but the degree of danger is ill-defined. A concentration of about 50 ppm is said to cause loss of fighting efficiency and one of 100 ppm to incapacitate and to be intolerable. The data were apparently obtained by observation of the effects of chlorine on man. The basis of the data is different, therefore, from those for lethality to man derived from animal experiments. They include presumably the effects of any enhancement of activity which may have occurred.

Zielhuis [12] has made proposals for Emergency Exposure Limits (EELs) for chlorine. His values are 7, 5, 4 and 3 ppm for exposures of 5, 15, 30 and 60 min, respectively. The National Academy of Science — National Research Council [13] proposals for Public Emergency Limits (PELs) are 3, 2 and 2 ppm for exposures of 10, 30 and 60 min, respectively.

Vulnerable members of the population

So far consideration has been limited to the effect of toxic gas on healthy adults. A significant proportion of the population, however, is more vulnerable. It is necessary to distinguish, therefore, between the less vulnerable, or regular, population and the more vulnerable, or simply vulnerable, population, which together make up the general, or average, population. The estimation of the concentration of chlorine lethal to the vulnerable population is another difficult aspect of this work. There appears to be little information available in the literature. It is important, however, because the vulnerable population is likely to contribute a relatively large proportion of the fatalities at the lower concentrations. A large part of a toxic gas cloud will be at these concentrations.

The population at risk around a hazard source varies appreciably with

TABLE 2

Proportion of people vulnerable to toxic gas hazard (after Hewitt [14])

	No. per 1000 people
Children <6 months	8
<12 months	8
12 months—5 years	75
5 years—9 years	82
Old people >70 years	85
People with chronic heart trouble	5
People with respiratory illness	9
People with restricted mobility	4
Blind people	2
Healthy youngsters and adults	722

TABLE 3

Relation between lethal concentration of chlorine for general population and vulnerable population (after Eisenberg et al. [15])

Effect	Deaths	
	General population (%)	Vulnerable population (%)
Severe harassment with some risk	0	25
Lethal	3	50
Lethal	50	100

the time of day. The vulnerable population is more likely to be at home during the day and thus constitute a relatively large proportion of the daytime population. Nevertheless, the vulnerable population is not synonymous with the daytime population. The treatment given here is limited to consideration of the vulnerable population.

The principal categories of vulnerable people are children, old people and people with respiratory or heart disorders. The less vulnerable members of the population are healthy youngsters and adults. An estimate of the proportion of people in the different vulnerable categories in the U.K. has been made by Hewitt [14] in the context of the assessment of toxic gas hazards. The values are shown in Table 2. A rough value for the proportion of vulnerable people is therefore 25%. More accurate estimation is beyond the scope of this paper.

One approach which has been used in hazard assessment is that of Eisenberg et al. [15], who used for chlorine and ammonia the relations between the general population and the vulnerable population given in Table 3. There are several points which should be noted in connection with Table 3. General population is not well defined, particularly as to whether or not it already includes the vulnerable proportion. The relations given in Table 3 imply a separate probit equation for the vulnerable population. The probit equation given by these workers for the general population is eqn. (12) of Ref. [1]. For this population the values of the causative, or injury, factor $\Sigma C^{2.75} T$ are

$\Sigma C^{2.75} T$	Lethality (%)
15.71×10^4	50
47.78×10^4	100 (say 99.9)

Then using these values to derive a further probit equation for the vulnerable population gives the equation

$$Y = -28.28 + 2.78 \ln \Sigma C^{2.75} T \quad (1)$$

But a probit equation of this form is equivalent to a lognormal distribution and the second constant in eqn. (10) of Ref. [1] ($= k_2$) is equivalent to the reciprocal of the spread parameter σ (σ^2 = variance) of that distribution. Thus the assumption implicit in the relations given in Table 3 is that the spread is less for the vulnerable than for the regular population.

Another treatment of a vulnerable population is the work of Hushon and Ghovanlou [16], who have studied the effect of a release of methylene chloride on a vulnerable population, but this study is highly specific and does not appear to be readily transferable to other cases.

The vulnerability of part of the population may be handled either by treating the whole population as a single homogeneous population with vulnerable members or by treating the regular and vulnerable sections as two populations. In the first approach there is a single distribution, whereas in the second there are two separate distributions with distinct modal values. It is not self-evident which approach is most likely to fit such data as may exist, but it is clear that for hazard assessment it is more convenient to handle the vulnerable population separately and to have a separate distribution applicable to that population. This is therefore the approach used here. It may be noted, however, that if two distinct distributions are used, they do not in general yield a distribution of the same type for the average population. Specifically, if the distributions for the regular and vulnerable populations are both lognormal, that for the average population cannot be expected to be lognormal.

Lethal load function

As described in the previous paper, the lethal toxic load function may be cast in two different but equivalent forms as follows:

$$L = ct^n \tag{2a}$$

or

$$L^* = c^m t \tag{2b}$$

with $m = 1/n$. It is a matter of indifference which expression is used to define the toxic load which causes a single, specified degree of injury; both give the same numerical results. In principle, it would be possible to distinguish between the two forms if one fitted better than the other the load—mortality distribution generally used, but in fact the distribution almost universally used for intensity—injury relationships in hazard assessment, not just for toxic gases but also for fire and explosion, is the lognormal distribution. With this distribution if L is lognormally distributed, so is L^*. Similarly, in the corresponding probit equation, given as eqn. (10) of Ref. [1], use of L^* instead of L is equivalent to multiplying the constant k_2 by n. Thus it is not possible to distinguish between the two forms.

Nevertheless, there are other arguments. From the point of view of hazard

assessment, in which it is usually necessary to integrate the lethal load function, the definition of load given in eqn. (2b) in the form

$$L^* = \Sigma C^m T \tag{2c}$$

is the more convenient. Since the paper is concerned with the estimation of the effect of toxic load for use in hazard assessment, it is this form which is used in the probit equations derived here.

It is believed, however, that there are also arguments for the alternative form. Here toxicokinetic models appear relevant, since although no modelling of the effects of chlorine has been found, the principles appear relevant to some other toxic gases which act not as respiratory irritants but as toxins in the body fluids and for which lethal load expressions of the form of eqn. (2a) have been quoted. Thus a one-component model for the body fluid concentration of the toxin with first order excretion and constant gas concentration is equivalent to a first order exponential stage with a step input, which gives a concentration rise of the form $[1 - \exp(-kt)]$, where k is a constant. It may be significant that this exponential rise may be approximated by a suitably scaled expression in $t^{1/2}$. Hence the argument from possible toxicokinetic modelling may favour the form given in eqn. (2a). It is possible that some form of first order model may also apply to damage done to the lungs by chlorine and that this may explain the observed effect of time which has been correlated in this work by taking $ct^{0.5}$ = constant.

The lethal load functions used for chlorine in this paper are therefore as follows:

$$L = CT^{0.5} \tag{3a}$$

and

$$L^* = \Sigma C^2 T \tag{3b}$$

but it is the latter which is used in the probit equations.

Concentrations lethal to man

On the basis of the material just described it is possible to make an estimate of the concentration of chlorine which is lethal to man. The approach adopted is to consider first the concentration which is lethal at the 50% level for an exposure period of 30 min, the effect of varying the concentration with the exposure period constant and the effect of varying the exposure period with the concentration constant, to determine from these the form of the lethal load function L and hence the LL values. Other features such as enhanced physical activity and vulnerable population are then considered and probit equations are derived.

The basic proposition is that in estimating the lethal toxicity of chlorine to man the most weight should be given to the work of Underhill [2] on dogs as shown in Table 3 and Fig. 2 of Ref. [1], but that these data should

be interpreted in the light of the other animal experiments shown in Tables 6 and 7 and Figs. 4 and 6 of that paper.

Taking all these data into account, the proposed lethal concentrations for man for the regular population with the base level of physical activity for a 30 min exposure period given in Table 4, Section A, are obtained. The LC_{50} is 500 ppm and the slope of the line corresponds to a ratio LC_{90}/LC_{10} of 4. This compares with an LC_{50} of 650 ppm and a ratio of 3.8 in Underhill's work.

The LC_{50} value proposed is therefore less than that for Underhill's dogs. It might reasonably be argued that since the LC_{50} appears from the animal experiments to increase with body weight, the value for man should be more, not less. On the other hand, Underhill's work represents only one set of experiments and the work on mice shows how much variability there can be between different experimenters studying the same animal. It is emphasised that the value chosen is intended as a best estimate and not a conservative one.

Another factor which should be taken into account is inhalation rate. For a lung irritant gas such as chlorine a suitable measure of the rate at which damage is done to the lung would seem to be the alveolar minute volume per unit area of alveolar surface. The value for man is approximately twice that for dogs. The use of an LC_{50} of 500 ppm for man as against one of 650 ppm for dogs make some allowance for this factor.

The respiration just described is the normal breathing of dogs and man. It is also necessary to consider the respiratory response of the dogs in the experimental work. According to Underhill [2], when first exposed the animals were irritable and excited, but later their breathing became laboured. Overall the effect of exposure on the respiration rate of dogs appears to show no marked trend [17]. It does not, therefore, appear necessary to make any special allowance for this factor.

This estimate of the lethal concentration needs, however, to be severely qualified. It applies only if man reacts in a passive manner similar to that of the dogs in Underhill's work. If the reaction is more active, the value of the lethal concentration needs to be modified accordingly.

Lethal load LL_{50}

An estimate of the lethal load LL_{50} at the base level of activity then follows directly. The concentration lethal at the 50% level for an exposure period of 30 min has been taken as 500 ppm. Hence

$$LL_{50} = CT^{0.5} = 500 \times (30)^{0.5} = 2{,}739 \text{ ppm min}^{0.5} \quad (4)$$

Other lethal loads

Similarly the toxic loads lethal at the 10% and 90% levels are 1,369 and 5,477 ppm $\text{min}^{0.5}$, respectively.

TABLE 4

Concentration of chlorine proposed as lethal to man for an exposure period of 30

A. Regular Population: Base Level of Physical Activity

Concentration (ppm)	Mortality (%)	Toxic load $CT^{0.5}$ (ppm $min^{0.5}$)
250	10	1,369
500	50	2,739
1,000	90	5,477

B. Vulnerable Population: Base Level of Physical Activity

Concentration (ppm)	Mortality (%)	Toxic load $CT^{0.5}$ (ppm $min^{0.5}$)
100	10	548
200	50	1,095
400	90	2,191

C. Regular Population: Standard Level of Physical Activity

Concentration (ppm)	Mortality (%)	Toxic load $CT^{0.5}$ (ppm $min^{0.5}$)
125	10	685
250	50	1,369
500	90	2,739

D. Vulnerable Population: Standard Level of Physical Activity

Concentration (ppm)	Mortality (%)	Toxic load $CT^{0.5}$ (ppm $min^{0.5}$)
50	10	274
100	50	548
200	90	1,095

E. Average Population: Standard Level of Physical Activity

Concentration (ppm)	Mortality (%)	Toxic load $CT^{0.5}$ (ppm $min^{0.5}$)
80	10	438
210	50	1,150
465	90	2,547

Vulnerable population

As stated earlier, there is little information available on which to base an estimate of the concentration lethal to the vulnerable population.

A possible starting point, however, is the minimum concentration at which a fatality has been observed. In the experimental work on animals described above, there was no fatality at a concentration below 50 ppm for an exposure time of 30 min. The nearest approach was a single fatality at 62 ppm in Schlagbauer and Henschler's [18] work. It is proposed that at the base level of activity a value of 100 ppm be taken as the concentration lethal to 10% of the vulnerable population for an exposure time of 30 min and that the same proportionality be applied to obtain the concentrations lethal at the 50% and 90% levels, which then gives these as 200 and 400 ppm, respectively. These lethal concentrations are given in Table 4, Section B. If these concentrations are compared with those for which physiological response data for man are available, as given in Table 12 of Ref. [1], the concentration of 100 ppm is about four times that which causes coughing and equal to that which is intolerable or incapacitating.

This approach implies the use of a concentration—mortality line of the same slope as that for the regular population. This assumption is made because there appears to be no good reason to vary the slope either way.

Levels of physical activity

Different levels of physical activity give different inhalation rates. It is proposed that the level of physical activity be defined in terms of the inhalation rate. In particular, since the base level of activity considered so far corresponds to rest, it is necessary to define another, standard level which is applicable to most daytime activity. On the basis of the data given in Table 1 it is proposed that this standard level of activity be taken as corresponding to an inhalation rate of 12 l/min. This compares with an inhalation rate of 6 ml/min at the base level of activity.

Inhalation rate factor

For the regular population it is proposed that the level of activity be taken as the standard level. However, if there is reason to expect that members of this population will deliberately minimise their physical activity, perhaps by remaining still indoors as a result of emergency planning advice, the level of activity may be taken as the base case. Conversely, if it is expected that the level of activity will be higher than the standard level, perhaps as a result of running through a gas cloud, an enhanced level may be used.

For the vulnerable population it is proposed that the treatment be similar with base and standard levels of physical activity. It is suggested, however, that for half the vulnerable population a base level of activity should not be used even in cases where it is used for the rest of the population, unless

there is good reason to do otherwise, since this part of the population is probably less likely to obey any instructions issued to minimise activity.

An inhalation rate factor ψ_1 has been defined which is the ratio of the inhalation rate at the actual level of activity to that at the base level (6 l/min). This factor is applied directly to the inhaled concentration. For the standard level of activity, $\psi_1 = 2$. The values of the lethal concentration for a 30 min exposure time for both the regular and vulnerable population for the standard level of physical activity are given in Table 4, Sections C and D, respectively. The values in Sections C and D are obtained by dividing by ψ_1 (= 2) the values in Sections A and B, respectively.

The proportionality assumed between inhalation rate and gas absorption rate, which is implicit in the use of the inhalation rate factor, may not hold at high inhalation rates. It is intended that the correction for inhalation rate by the use of the factor in the form given should not be used for inhalation rates which exceed the base value by a factor of more than 4.

Lethal concentrations

The lethal concentrations proposed for both regular and vulnerable populations and for both base and standard levels of physical activity for a

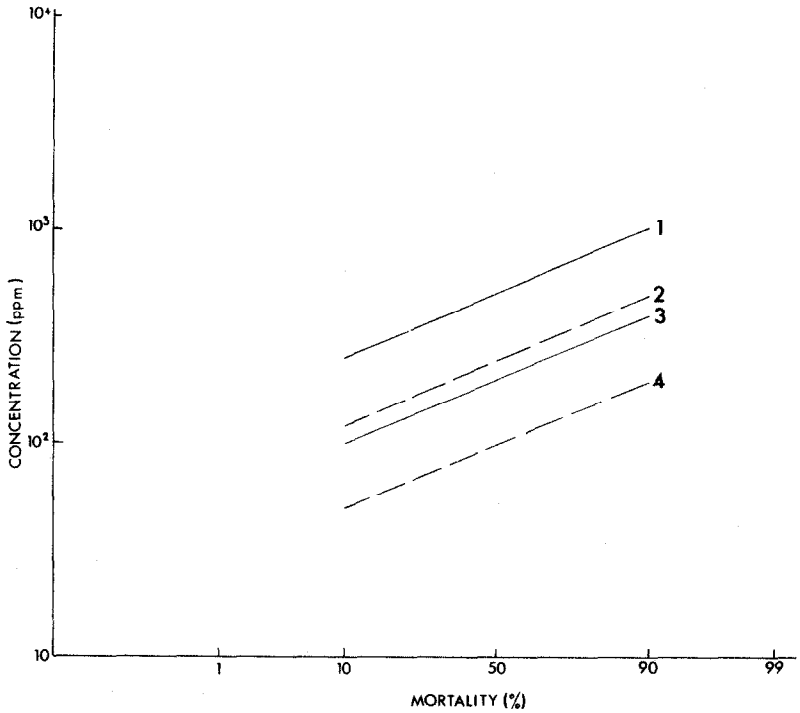

Fig. 1. Concentration of chlorine proposed as lethal to man for an exposure period of 30 min. Line 1, regular population, base level of activity; line 2, regular population, standard level; line 3, vulnerable population, base level; line 4, vulnerable population, standard level.

30 min exposure period are shown in Table 4 and are plotted in Fig. 1. From the plot in Fig. 1 it is possible to estimate the lethal concentrations for an average population drawn 75% from the regular and 25% from the vulnerable population. These are shown in Table 4, Section E.

The lethal concentrations proposed for both regular and vulnerable populations for the standard level of physical activity for a 10 min exposure time are shown in Table 5, Sections A and B. These values are derived from those in Table 4, using equation (3a). The values given in Table 5 are plotted in Fig. 2. Lethal concentrations for the average population are given in Table 5, Section C.

As explained above, the lethal concentrations for the average population given in Table 4, Section E and Table 5, Section C, do not plot as straight lines on log probability paper and therefore cannot be fitted to a lognormal distribution or a probit equation.

Probit equations

The following probit equations may be derived from the data given in

TABLE 5

Concentration of chlorine proposed as lethal to man for an exposure period of 10 min

A. Regular Population: Standard Level of Physical Activity

Concentration (ppm)	Mortality (%)	Toxic load $CT^{0.5}$ (ppm $min^{0.5}$)
217	10	685
433	50	1,369
866	90	2,739

B. Vulnerable Population: Standard Level of Physical Activity

Concentration (ppm)	Mortality (%)	Toxic load $CT^{0.5}$ (ppm $min^{0.5}$)
87	10	274
173	50	548
346	90	1,095

C. Average Population: Standard Level of Physical Activity

Concentration (ppm)	Mortality (%)	Toxic load $CT^{0.5}$ (ppm $min^{0.5}$)
139	10	438
364	50	1,150
805	90	2,547

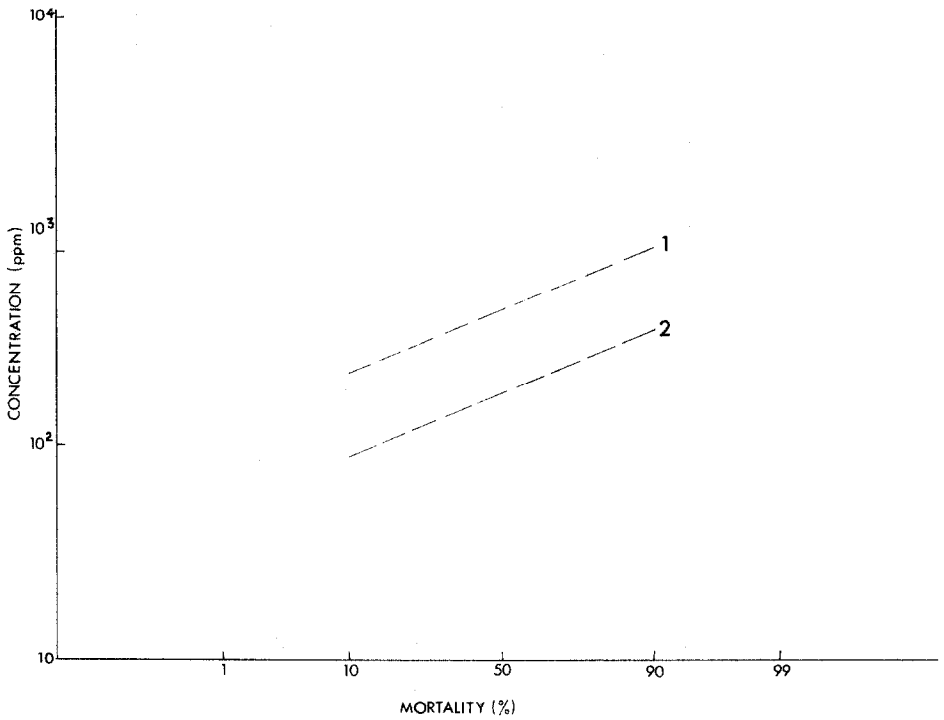

Fig. 2. Concentration of chlorine proposed as lethal to man for an exposure period of 10 min. Line 1, regular population, standard level of activity; line 2, vulnerable population, standard level.

Table 4:

Regular Population

Base Level of Physical Activity

$$Y = -9.57 + 0.92 \ln \Sigma C^2 T \quad (5)$$

Standard Level of Physical Activity

$$Y = -8.29 + 0.92 \ln \Sigma C^2 T \quad (6)$$

Vulnerable Population

Base Level of Physical Activity

$$Y = -7.88 + 0.92 \ln \Sigma C^2 T \quad (7)$$

Standard Level of Physical Activity

$$Y = -6.61 + 0.92 \ln \Sigma C^2 T \quad (8)$$

These probit equations are compared with those given in the literature in Table 6.

Very high concentrations

In general, the injurious effect of a toxic gas is a function both of concentration and of time, but there may be a limiting value of the concentra-

TABLE 6

Probit equations for chlorine

A. Literature Equations for Fatality

		Lethal concentration for 30 min exposure period		
		LC_{10} (ppm)	LC_{50} (ppm)	LC_{90} (ppm)
Eisenberg et al. [15]	$Y = -17.1 + 1.69 \ln \Sigma C^{2.75} T$	26	34	44
Perry and Articola [19]	$Y = -36.45 + 3.13 \ln \Sigma C^{2.64} T$	36	42	49
Rijnmond Report Industrial Comment, Harris and Moses [20,21]	$Y = -11.4 + 0.82 \ln \Sigma C^{2.75} T$	237	418	738
ten Berge and van Heemst [22][a]	$Y = -5.04 + 0.5 \ln \Sigma C^{2.75} T$	170	430	1,093

B. Proposed Equations for Fatality, Standard Level of Physical Activity

	Lethal concentration for 30 min exposure period		
	LC_{10} (ppm)	LC_{50} (ppm)	LC_{90} (ppm)
Regular population: $Y = -8.29 + 0.92 \ln \Sigma C^2 T$	125	250	500
Vulnerable population: $Y = -6.61 + 0.92 \ln \Sigma C^2 T$	50	100	200
Average population	80	210	465

C. Literature Equations for Injury

Eisenberg et al.	$Y = -2.40 + 2.90 \ln C$
Perry and Articola	

[a] Original equation

$Y = -6.5 + 0.5 \ln \Sigma C^{2.75} T$

where C is concentration (mg/m^3) and T time (min).

tion at which other factors come into play so that at this level it is concentration only which matters. It is not clear whether this is so for chlorine or at what level it may occur. The evidence from gas warfare suggests, however, that if there is such an effect, the concentration at which it occurs is very high.

Henderson and Haggard [3, p.132] state that a concentration of 1,000 ppm is rapidly fatal for a short exposure. On the other hand they give a lethal concentration for a 10 min exposure as 1,926 ppm. Prentiss [5] gives

a similar value. As discussed earlier, it seems probable that this figure is intended as the LC_{90} value.

If the probit equation for the regular population for the standard level of activity, given as eqn. (6), is considered, then a mortality of 90% is obtained at a concentration of 1,900 ppm for an exposure time of about 2 min. As a first approximation, therefore, the probit equation proposed gives an estimate which appears reasonable and seems unlikely to seriously underestimate the mortality even at very high concentrations.

Acute death factor

From the lethal load the mortality may be estimated using the probit equation. As described in the previous paper, the proportion of acute deaths is a function of the mortality. From analysis of war gas casualties an estimate may be made of the proportion P_a of acute to total deaths, or acute death factor, as follows:

$$P_a = 0.8 + 0.2P \quad (9)$$

Medical treatment factor

The allowance which should be made for the reduction in delayed deaths due to appropriate medical treatment, compared to total neglect, is unclear, but is almost certainly high for the regular population. It is stated in *Diseases of the War* [23, p.386] that even in the early days the fatality rate for such cases was less than 50%, while Underhill [2, p.149] says that with proper treatment the number of recoveries (in his terminology, not dying at all) should equal the number of survivals (not dying in the acute stage). It seems probable, however, that medical treatment may not be quite so effective in reducing the mortality of the vulnerable population.

On the basis of these arguments it is proposed that the medical treatment factor ψ_2 be taken as 0.9 and 0.7 for the regular and vulnerable populations, respectively. This means that for the regular population, for example, good medical care will convert some 90% of the potential delayed deaths into recoveries. These are necessarily approximate estimates, but their overall effect on the mortality is not great, since most deaths are acute rather than delayed.

It is not, of course, appropriate to claim credit for the mitigating effect of medical treatment unless there exist the organisation, the expertise and the facilities commensurate with the accident envisaged. The number of people who may have to be treated after a chlorine release is likely to be many more than the number of potential fatalities.

Methodology for hazard assessment

The overall methodology proposed for the estimation of the mortality from an accidental chlorine release given the concentration—exposure time data may be summarised as follows.

A straightforward estimate of the mortality for the regular and vulnerable populations with standard level of activity may be obtained using eqns. (6) and (8), respectively.

If it is desired to produce an estimate which takes account of other conditions and makes at least some allowance for the other factors discussed the approach is as follows:

1. Estimate the inhalation rate factor and apply it to concentration
2. Estimate the toxic load using the corrected concentration
3. Calculate the uncorrected mortality, estimate the acute deaths factor and apply it to this mortality
4. Estimate the medical treatment factor and apply it to the proportion of potential delayed deaths
5. Calculate the corrected mortality

It is not supposed that any great increase in accuracy is achieved by the application of this methodology and it may be questioned whether its use is justified or whether simple application of eqns. (6) and (8) is not sufficient. The methodology has been presented, however, because it is believed that it is always desirable to make a best estimate and to take into account relevant additional factors.

Discussion

A set of values has been derived for the concentration of chlorine lethal to man for use in the assessment of major hazards and a methodology has been given for applying these values to obtain an estimate of the mortality. Separate values are given for the regular and vulnerable populations and for different levels of physical activity.

The value proposed for the lethal concentration LL_{50} of chlorine for a regular population is based primarily on Underhill's work [2] on dogs but takes into account the other animal work. It is much higher than the value given by Eisenberg et al. [15] and agrees more closely with the values suggested by recent critics of that work [20 (industrial comment), 21, 22, 24].

There are, however, important qualifications. First, there is a separate relation for the vulnerable population. Second, it is intended that the crude toxic load be modified to allow for enhanced physical activity. The effect of these features is to reduce significantly the LL_{50} for the average population. Third, there is an adjustment to the crude mortality to allow for medical treatment, but the compensating effect of this is slight. The value proposed for the lethal concentration for the vulnerable population is based primarily on the work on animals, but account has also been taken of non-lethal human responses. It is subject to greater uncertainty than that for the regular population. The relations given for the lethal concentrations have been derived from data with exposure periods mainly in the range 10—30 min and are not intended to be used for exposure periods outside this range.

The method of allowing for the effect of exposure period, and in partic-

ular the rather mechanistic method of summing the loads at a number of exposure times to obtain an overall load, is not satisfactory, although it is the best which can be done at present. There appears to be need for a more fundamental approach based on a physiological model.

The degree of error in the use of the probit equations is difficult to estimate. The confidence limits on Underhill's work vary somewhat depending on the way in which they are calculated. The applicability of this work is itself a matter of judgment. Further, the confidence falls off rapidly at low mortalities, particularly below about 10%.

In a hazard assessment the mortality at low gas concentrations is particularly important, because, taking into account both outdoor and indoor exposures, a large proportion of the area, and hence of the population, affected will be exposed to these low concentrations. Unfortunately, it is precisely at these low concentrations that the potential error is greatest, both because of the wider error bounds on the relation for the regular population and because of the greater uncertainty in the values applicable to the vulnerable population.

Attention is drawn to two additional piece of information described in the previous paper, both of which point to lower lethal concentrations in certain circumstances. One is a set of experiments in which mice exposed for 3 hours to concentrations of chlorine as low as 10 ppm had high mortalities. The other is the evidence that if the level of activity of an animal is very high, death may occur immediately as a result of oxygen deficiency in the blood.

The estimates of chlorine toxicity derived in this work are based upon a number of assumptions and are necessarily tentative. There are several aspects which would benefit from further investigation. These include in particular the form of the lethal load function with special reference to the time effect, the feasibility of a toxicokinetic model, the effects of very low and of very high concentrations, the vulnerable population, the proportion of acute deaths and the effectiveness of medical treatment.

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List of symbols

The symbols used are as in Reference [1] plus

k constant

P_a probability of acute death
ψ_1 inhalation rate factor
ψ_2 medical treatment factor

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