ASPECTS OF SAFETY LIMITS IN INDUSTRY

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· INTRODUCTION

Toxic materials will be used in industry in increasing quantities. It is, therefore, the duty of the industrial physician to guarantee safe working conditions under all circumstances in order to prevent disease, and to avoid any unfavourable influence on the life-span and health of the persons exposed and of their offspring. This duty extends not only to the average working conditions of healthy people; peak concentrations caused by mistakes, leakages, *etc.*, and the exposure of workers with some chronic disease or special susceptibility, should also be considered, and safety should, as far as possible, be guaranteed even under these unfavourable conditions.

A certain number of risks must be accepted in life (traffic!), and it might be stated that absolute safety cannot be realized from a practical or, especially, from an economic point of view. The worker however, for economic reasons has, as a rule, no free choice concerning his environmental conditions, and, therefore, it is the industrial physician who has to take over the responsibility as an adviser to the management. For these reasons, he can never accept conditions that are on the borderline between safety and danger; he should claim a *safety factor* large enough to answer reasonable health demands. There is no way of arriving at any objective exact estimation of the necessary safety factor; it is a matter of (international) deliberation and agreement.

It is worthwhile to compare these industrial health demands with those put forward by nutritionists. Many chemicals are considered as acceptable additives to food (for purpose of sterilization, staining, *etc.*). Now what are the criteria used in this field? LD_{50} should not show considerable variation in different types of animals, the mortality-increasing dose curve should be steep (this means, that there will be no great variability of toxic action in different individuals of the same sort of animal), no cumulative effect should be present, and the compound used should have a toxicity less than indicated by an oral LD_{50} of 1 g/kg. Generally, chemicals that are approved in this way are accepted in a dose with a safety factor of 100; *i.e.*, only a daily intake of 1 per cent of the smallest dose that shows pathological reactions is accepted[1].

It is obvious that these very strict demands are not applicable to industrial toxicology, but, nevertheless, from a medical point of view, the industrial physician should try to reproduce these demands as far as possible. This is

especially true as far as the use of a safety factor is concerned in order to meet the requirements in unfavourable conditions as mentioned previously.

The size of this safety factor might depend on the type of toxic material concerned and should, in our opinion, be an important point of discussion at this symposium. In any case where maximum allowable concentration (M.A.C.) values or other safety limits are applied, the safety factor used should be clearly stated.

Discussion are still going on concerning the terms *maximum allowable* or *acceptable concentration*, *threshold value (limit)* or *hygienic standard* (or *safety limit*).

We propose to define *threshold value (limit)* as the largest concentration that does not, or is not expected to, produce any harmful effect or indication of pathological influence in well-observed groups of workers (healthy) during an indefinitely long period (many years or a lifetime), and giving no evidence of any harmful genetic consequence*. There is a great need for the publication of the results of observations on such groups[2], and for improving the methods used in these medical observations.

Accepting this definition, the following relation exists:

$$\text{Safety limit (hygienic standard)} = \frac{\text{threshold limit}}{\text{safety factor}}$$

General acceptance of these or similar definitions would, in our opinion, considerably diminish confusion in this field. We must confess, however, that much controversy is possible concerning the significance of a symptom or sign observed as an indicator of harmfulness. The difference between American and Russian figures on M.A.C. values seems for the greater part to depend on this interpretation.

CRITICAL REMARKS ON THE M.A.C.

" Threshold limits should be used as guides in the control of health hazards and should not be regarded as fine lines between safe and dangerous concentrations "†. When poisoning is airborne, only in very few cases is the relation $E = ct$ (E = effect, c = concentration in inspired air, t = time of exposure) more-or-less correct (*e.g.*, with $COCl_2$ and CO). Generally, the quantitative relations are much more complicated for these two reasons:

(a) a part of the inhaled substances is expired again, and in reality, does not enter the body;

(b) detoxication processes start when toxic material enters the circulation.

In its most simple form the relation could then be written as $P = (c_i - c_{ex}) \, tA - D$. The effect $E = f(P)$, and is some, more-or-less complicated, function of the amount of toxic substance P remaining in the body. In this formula c_i and c_{ex} represent the concentrations in inspired and expired air respectively, t = time of exposure and A = the average respiratory minute volume. D represents the sum of all detoxication processes.

* This definition is principally in accordance with Glömme's definition, XII Intern. Congr. on Occupational Health, Helsinki, 1957.
† Threshold limit values for 1958 (ref. 3).

When we try to describe this term D we run into rather involved problems of which, under certain conditions, an approximate mathematical description could be given by the following equations:

$$E = f(P);$$

$$P = (c_i - c_{ex}) tA - c_b e^{-d_{ex} t_d} - (c_{o_1} e^{-d_1 t_d} + c_{o_2} e^{-d_2 t_d} + \ldots c_{o_n} e^{-d_n t_d})$$

In this formula t = time of exposure, A = respiratory minute volume, d_{ex} = detoxication constant for removal of toxic substance by the lungs, c_b = concentration of toxic substance in blood, t_d = detoxication time, $c_{o,1}$, $c_{o,2}$ and $c_{o,n}$ = concentration of toxic substance in different systems such as kidney, liver, bones, *etc.*, $d_1 \ldots d_n$ = detoxication constants. The supposition is made here that detoxication is a process following an exponential course; however, different relations are possible. Cumulative effects, *i.e.* the formation of more-or-less harmful depôts, and complicated processes such as the formation of toxic substances within the body, are all contained in differences in the function f in the equation $E = f(P)$. The main purpose of these theoretical mathematical considerations is to prove that the acceptance of c_i as an index for the measurement or semi-quantitative description of toxic action must be fallacious in many cases.

There are other reasons for criticizing the value of M.A.C.; they have been discussed previously by a number of authors, and do not need to be repeated here.

We fully agree with the statement made by the I.C.I. Industrial Products and Health Research Unit[4] that: " The concept of maximum permissible concentration has little validity; it is a dangerous concept and based on misunderstanding ". We want to add that it is not justified to accept exclusively a wrong concept as a basis for practical actions simply because it is so simple. What we should try to describe in figures is reality, even when it is complicated.

However, we must confess that the use of M.A.C.'s is so widespread that we should not be able to stop using them now. Though Miriam Sachs is right in stating[5] that we should use some yardstick even if it is only a rubber yardstick, we are of the opinion that it is not sufficient to try to describe a rather complicated process with one simple figure that has, in fact, a far too decisive value in the praxis of occupational health.

This conclusion is the more important because, as Smyth[6] points out in a considerable number of cases, no safety factor at all is applied when setting up the M.A.C. of different substances.

Laymen (lawyers, engineers, managers) are making use of M.A.C. values in a way which must be considered as unjustified. This is another and a very sound reason for being extremely careful in this matter, and for adding to the M.A.C. values a number of other quantitative data and experimental observations which will be discussed later on.

NEEDS OF INDUSTRIAL PHYSICIANS AND INDUSTRIAL HYGIENISTS

Practical workers in the field of Occupational Health need conclusive information concerning the toxicity of products used in industry, and

information regarding the bases on which safety limits (hygienic standards) are to be accepted, applied and executed. This information should be made available to them in a concise, surveyable form, and should not suggest unjustifiably exact precision. The data should not give real or " would be " arguments to laymen, and should stimulate those concerned to achieve the best possible, instead of acceptable, conditions within the limitations of reasonable economy.

The list required should give a number of well-defined facts and observations in order to make it possible for the trained industrial physician to evaluate approximately the risks under different working conditions, and to set up an effective and efficient programme of periodical examinations in order to guarantee the safety and health of the workers for whom he is responsible.

Finally, the data should clearly indicate where there is lack of knowledge, and the need for further study and observation. The information should clearly show that, in toxicology, we are not using well-defined solid yardsticks, but rather elastic ones, indicating only the trend of our claims and wishes.

LIST OF SAFETY LIMITS (L.S.L.)

It is suggested that a list of safety limits be compiled, edited by some international authoritative organization, e.g., a Standing International Toxicological Expert Committee set up by the Permanent Committee and International Association on Occupational Health in co-operation with I.L.O. and W.H.O.

The composition of this list certainly will be much more difficult than the publication of a M.A.C. list. However, it is our opinion that the importance of the L.S.L. can hardly be exaggerated, and would be an invaluable source of information for industrial physicians throughout the world. It is a real challenge to those interested in industrial medicine today. This great importance would justify the necessary effort. The international committee in charge could eventually appoint a number of subcommittees, each in charge of the collection of data concerning a certain group of industrial poisons. Regular revision of the L.S.L. would be required as a matter of course.

Just as a preliminary proposal, and in order to explain our line of thought, we present in *Table 1* an example of a solution to the problem which we have stated. It is clear, however, that many deliberations and discussions would be needed before a final form for an L.S.L. could be established.

As a general principle, we followed the suggestion of Drinker[7] in making a number of classes of concentration (in parts/million). We think, however, that for our purpose more than the 6 classes suggested by Drinker are to be recommended. This could be done by applying a more or less logarithmic scale; ten classes are thus suggested.

Table 1 suggests data to be given in the L.S.L.

In the first part of the table, A_1, A_2, B, etc. (representing the values defined) can be placed in their proper places, mentioning in brackets the observed or estimated concentrations.

Table 1

Part 1. Scale of toxicity

Class	1	2	3	4	5	6	7	8	9	10
Concentration in p.p.m.	$<0\cdot1$	$0\cdot1-1\cdot0$	$1\cdot0-10$	$10-50$	$50-100$	$100-250$	$250-500$	$500-1000$	$1000-3000$	>3000
Name of product and chemical composition		Figures in brackets in p.p.m. v/v								
X				A_1 (......) A_2 (......)		B_1 (......)	B_2 (......)	C (......)	D (......) E (......)	F_1 (......) F_2 (......) F_3 (......)
Y			A_1 (......) A_2 (......)		B_1 (......) B_2 (......)	C (......) D (......) E (......)	F_1 (......)	F_2 (......) F_3 (......)		

Part 2. Other information

1	Recommended safety factor			5	6	7
	2	3	4			

A_1 and A_2 the highest and lowest M.A.C. values suggested in the literature by some authoritative body.

B_1 and B_2 threshold limit (man) (highest and lowest value)

C Early signs and symptoms (man); quantitative limits of signs: *e.g.* haematoporphyrinuria, trichloroaceticacid, *etc.*

D Disease (signs and symptoms to be mentioned)

E Serious disease with loss of working capacity (signs and symptoms to be mentioned).

Lethal poisoning (by chronic exposure)

F_1 Peak concentration causing serious disease (by acute exposure)

F_2 Peak concentration causing death (by acute exposure)

F_3 Peak concentration causing death (by acute exposure)

1 LD diagram (to mention types of animals used)
2 Recommended safety factor for " normal " people
3 Recommended safety factor for sick people (type of illness to be mentioned)
4 Recommended safety factor in case of oversensitiveness (allergy, or for combination with other toxic substances (*e.g.* alcohol)
5 Some physical data
6 Recommended safety limit
7 Special remarks and basic literature concerning figures given in the list

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It is obvious that very toxic substances show a " shift to the left ", whereas the danger of surpassing average M.A.C. values can be approximately estimated by the distance in the scheme between A and B (or C and D), whereas the position of F_1 and F_2 indicate the danger of leakage and careless working methods.

References

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