

ANALYTICAL METHODS FOR MEASURING THE CONCENTRATIONS OF TOXIC SUBSTANCES IN INDUSTRIAL ATMOSPHERES

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The relation between maximal allowable concentrations (M.A.C.'s) and the analytical methods used to measure the contamination of industrial atmospheres, is reminiscent of the old problem, "which came first, the chicken or the egg?" Does the analyst need information on the magnitude of these limiting concentrations before he can select and test a suitable quantitative method, or does the industrial toxicologist require the analytical information on factory atmospheres before he can decide on the limit?

The answer to this question lies in the methods used to establish the M.A.C.'s, and which are being extensively discussed by other Sections of this Symposium. The origins of the 223 figures in the 1955 list of threshold limits issued by the American Conference of Governmental Industrial Hygienists, have been reviewed by Stokinger. He has shown that 42 per cent are based on animal experiments, 11 per cent on human experiments, while 4 per cent have the support of both, and 9 per cent are based on what has been termed the "educated guess", with the origins of 1 per cent uncertain. The remaining 33 per cent derive from industrial experience and, of these, 10 per cent also have the support of animal experiments. Now it is, evident that with this 33 per cent, the observed toxic effects on man must have been correlated with the quantitative figures of atmospheric contamination obtained by the analyst, before a decision was made on the magnitude of the threshold to be selected. The analytical methods must, therefore, have existed prior to the publication of the threshold limits, and acceptance of these limits as valid implies that the analytical methods used are regarded as satisfactory and that they have been applied in a proper manner.

On the other hand, a knowledge of the magnitude of the M.A.C.'s is essential to the analyst in the selection of suitable methods for industrial air analysis. When a method of this type is requested, the most important question, is "what order of concentration is to be measured, and with what precision are the results required?" Few sensible toxicologists would demand a high degree of precision, for they know only too well the uncertainty which surrounds much of the evidence on which these threshold limits are based, and they would realise that a precision of 20 per cent would be adequate, but that it is essential that the agreed level of precision should be achieved, however low the M.A.C. may be. It would be true to say that it

is not possible to publish a useful analytical method for an atmospheric contaminant, unless some indication of the M.A.C. is available.

Not only has the M.A.C. an influence on the design of an analytical method, but, in at least one respect, the attitude of the analyst has exerted some influence on the approach of the industrial hygienist towards these limits. In recent years there has been a considerable body of opinion antagonistic to the concept of M.A.C., much of this objection centring round the term "allowable". Not only has it been considered improper to give a legal connotation to such indefinite figures, but it has also been held morally indefensible to allow a concentration of any magnitude at all in view of the slenderness of the toxicological evidence on which these figures are based. It has been considered that, so long as such allowed concentrations exist, they may be misinterpreted by those not fully informed on their nature, and that there will be no stimulus for factory managements and engineers to design and operate plant where the concentration in the atmosphere will approach the ideal value, which, in the opinion of those who think in this way, is zero. Pressure has been applied, in particular, to establish zero concentrations for known or suspected carcinogens, on the ground that there can be no certainty of a concentration which is harmless to man. However, from the point of view of the analyst, a zero concentration is meaningless. The lower limit of usefulness of an analytical method is controlled by the sensitivity of the method, by the volume of the air sample taken and by the magnitude of the blank value, which is largely a matter of the quality of the reagents. By using a sufficiently insensitive method and sufficiently impure reagents an analyst can make almost any atmospheric concentration show no significant difference from the blank, which is the only meaningful definition of a zero concentration. Conversely, if the analyst is given a definite concentration to aim at, even though it be as low as the minute value of 0.002 mg/m^3 suggested for beryllium dust, it is possible for him, by the selection of a sensitive method, by the collection of a large air sample and by careful attention to the purity of reagents and the cleanliness of glassware, to produce an answer with the agreed precision at this level.

An examination of the industrial hygiene literature shows a tendency towards a regular decrease in the values of M.A.C.'s. There is no evidence to attribute this to an increase in sensitivity of the working population, but it is due to a greater preoccupation with the more subtle effects of prolonged exposure and to the greater probability that hypersensitive individuals will be encountered with the more prolonged use of a chemical. In spite of this tendency, the purely analytical considerations make it desirable that the M.A.C. should always have a finite magnitude and never be placed at zero. Nevertheless, when the toxicological evidence is singularly incomplete or uncertain, and this applies particularly in the case of known or suspected carcinogens, it would be appropriate to annotate the figures with the comment that they are liable to be drastically reduced if fresh information becomes available.

It has already been stated that when M.A.C.'s are based on clinical experience, there is strong evidence that an analytical method has been used, though it may not be suitable for general routine use. Where the limits are based on controlled experimentation on animals or on man, it is not necessary

that a reliable analytical method should have been available. It is possible to prepare known test atmospheres for such toxicological investigations, and procedures for so doing are described in this Symposium. However, it is always preferable to check such atmospheres by analysis to avoid errors. It seems probable that, for a considerable number of substances appearing in published lists of M.A.C.'s, adequate and tested analytical methods have not yet been developed. If this is true, then the question might be asked, "of what value are these lists of limits when the absence of reliable analytical methods prevents their application to the control of industrial conditions?" It has already been stated that these limits are of great assistance to the analyst in the selection of suitable methods and their establishment should, where possible, precede the publication of analytical methods. Moreover, it is well-known that many of the limits are used as guides in the design of plant and process operation and in the enforcement of safety precautions, without analytical tests ever being made. For example, one code of practice may be established in a factory for substances with a limit in the region of 1,000 p.p.m., another for those at 100 p.p.m., and still more careful attention to plant design and more stringent enforcement of safety precautions when the M.A.C.'s are 10 and 1 p.p.m. While this practice is preferable to the complete disregard of all available toxicological information, it may fall into error as it is based on the assumption that M.A.C.'s can completely define the relative hazards between chemical substances, when other factors, such as volatility and skin penetration, also play an important part in determining the potential dangers.

The existence of M.A.C.'s without corresponding reliable analytical methods for the control of industrial atmospheres emphasizes the need, which still exists, for the investigation of such methods. It is, however, most important that this study should be undertaken by analysts fully conversant with the problems involved, and in close collaboration with industrial toxicologists familiar with the properties of the substances concerned. The design of an analytical method cannot be separated from the special problems which surround the measurement of contamination of a factory atmosphere. The concentration of a toxic substance in a factory will vary in space and time and cannot, as in a properly conducted experiment in the laboratory, be defined by a single figure. The design of the tests for investigating such an atmosphere must, therefore, be considered with care. The person undertaking or directing the investigation must make himself familiar with the nature of the manufacturing processes, the positions of highest risks, the movements of process and maintenance operators, and the air currents of the ventilation system. He must then apply his specialized knowledge so that the tests made give a reliable picture of the hazard from the atmospheric contaminant, with the minimal expenditure of time and effort. In order to achieve this, a decision must be made as to when, where, how often, and for how long the measurements should be made. In most published methods, the time required to collect the air sample is measured in minutes rather than in hours, and, with such methods, the variable nature of an industrial atmosphere may be investigated by a series of short tests. In some methods, a large air sample collected over a long period of time is convenient for purely analytical reasons, but the decision to make a test of

long duration should not be left entirely in the hands of the analyst. Some authorities prefer a test lasting perhaps the whole of the working shift, perhaps with the air sampling point attached to a worker as he moves in the course of his occupation. However, when men are exposed to a fluctuating concentration of a toxic substance, a detailed knowledge of its toxicological properties is necessary in order to decide whether the integrated concentration provides a reliable measure of the atmospheric hazard. Such considerations are the province of the industrial hygienist rather than of the pure analyst, and if direction concerning the duration of the sampling period is to be included in an analytical method, it should be made with the advice of someone well versed in the complexities of this subject.

The Toxicology and Industrial Hygiene Division of the International Union of Pure and Applied Chemistry, which organization is part sponsor of this present Symposium, is an example of a close collaboration by analysts and industrial toxicologists in the design of analytical methods for toxic substances in air. Its president, Professor Truhaut, is well known both as a toxicologist and an analyst, and he is also president of the Organizing Scientific Committee of this Symposium. The difficulties of obtaining agreement on the methods mentioned are considerable. As an example of this, one may quote the recent publication of methods for 10 substances by the American Conference of Governmental Industrial Hygienists, which is the outcome of 13 years' work by a series of expert Committees. The difficulties confronting the I.U.P.A.C. Division at an international level are even greater, and I, as secretary, am fully aware of the difficulties of transacting business by correspondence with personal meetings only every one or two years. This I.U.P.A.C. Division was established in 1947 and has already had its first findings published; this publication* includes methods for 21 substances, and a general Introduction describing the principles of air analysis and sampling procedures.

The Toxicology and Industrial Hygiene Division has drawn extensively on the scientific literature for its selection of methods, and on the knowledge and experience of its members and of those experts in several countries who have been kind enough to assist us in our work. Several guiding principles have influenced the choice and form of the methods adopted. I have already mentioned that the latter should be sufficiently sensitive to measure concentrations in the region of the M.A.C. with an acceptable precision. In addition to this, great emphasis has been placed on simplicity of operation; ideally the methods should be sufficiently simple not to require the services of a skilled analyst, for, on occasions, tests must be carried out at sites where laboratory facilities are primitive and technical skill lacking. A test which can be performed by a factory foreman, by a safety official or by a medical officer, without the necessity for a prior training in analysis, is much more likely to be applied than one which requires complicated apparatus and experience in chemical manipulations. Our Division has been aware that our main responsibility lies rather with the small factories and with those which use the products of the chemical industry, rather than with large organizations having efficient analytical laboratories; but it is also our experience

* *Methods for the Determination of Toxic Substances in Air*, published by Butterworths Scientific Publications, London (1959)

that even the latter would prefer tests which do not occupy the time of a skilled analyst.

Simplicity of operation, however desirable, should not be attained at the expense of specificity and precision. It is, of course, preferable that a method should not be affected by the presence of other substances in the atmosphere, although from an industrial hygiene viewpoint, an interference giving rise to an over-estimate is less serious than one which produces an under-estimate. An analytical method should also be capable of yielding a speedy result, as a delay of several hours in the recognition of a dangerous atmosphere is clearly undesirable. Sometimes it is not possible to find a method which conforms with all these guiding principles. It may be necessary to select one which calls for considerable technical skill, as in the determination of mercury vapour in air, or it may be necessary to sacrifice more specificity and precision than an analyst would prefer. For some atmospheric contaminants two methods have been selected; a simple, rapid, but not very precise procedure which is capable of giving a warning of excessive atmospheric concentrations, together with a more complex procedure capable of giving more reliable results.

The final selection of methods reached by any group of experts does not imply that other adequate methods do not exist, for the choice must inevitably be influenced by the personal experience of the members. The Toxicology Division is also well aware of two important groups of methods which are available commercially, and which are finding an increasing use in industry, and yet which are not, in the main, eligible for official adoption. The first group includes those methods using complicated instruments which give directly an indication, or a permanent record, of an atmospheric concentration. Such instruments are based on a variety of physical principles; ultra-violet and infra-red absorption, emission spectroscopy, thermal conductivity and ionizability. They usually have a high sensitivity and specificity and, provided that they are functioning properly and are correctly calibrated, they are very simple to use. Their advantages may outweigh the high initial cost and the need for skilled maintenance, yet it is not possible for such methods to be officially adopted when a complete specification of the apparatus is rarely available and details are frequently protected by patents. Moreover, the calibration of such instruments is entirely in the hands of the manufacturer, and it is rarely possible for the user to apply a satisfactory check. The second group includes methods which, with one exception, have not been adopted, yet which have much to commend them; these methods make use of what has been termed an indicator tube. This is a glass tube filled with a granular material impregnated with suitable reagents which, when an air sample is drawn through it, develops a coloured stain if the contaminant for which it is designed is present. The concentration in the atmosphere is assessed from the length of the stain for a given volume of air, or from the volume of air required to colour the whole of the reactive layer. A range of such tubes for the more usual industrial air contaminants is available commercially in several countries. However, as with the instrumental methods, the reluctance to adopt them officially is due to the secrecy of the manufacturers concerning formulation, and lack of control over calibration. The one exception is the most important indicator

tube for carbon monoxide which contains silica gel impregnated with palladium sulphite, two versions of which were developed during the war in the United States and Great Britain, and which subsequently have been described in detail. The adoption of more of these methods, which, on account of their simplicity, speed, and low cost, are ideal for industrial hygiene air analysis, must wait upon further publications describing formulation and giving a critical analysis of performance.

I do not propose to discuss any analytical methods in detail, but I think it appropriate to refer to two items of general interest. I have already mentioned that one disadvantage of commercial instruments or indicator tubes for industrial hygiene air analysis is that the results obtained are dependent on the efficiency of calibration. However conscientious a manufacturer may be, his apparatus will not be satisfactory if the test atmospheres which he uses for calibration have not the concentrations which he thinks they have. The procedures used for the preparation of known concentrations of toxic substances in air for the purpose of toxicological investigations have been described elsewhere in this Symposium. They have been adapted for checking the analytical methods, not only the commercial ones previously mentioned, but all those in which the toxic substance in an air sample is extracted by means of a liquid bubbler or other absorber prior to quantitative measurement. A dynamic method of preparing the test concentrations is much to be preferred to a static method, which frequently involves losses due to adsorption or decomposition, and does not readily permit the taking of an air sample. A wide range of concentrations may easily be prepared. There is no risk of chemical degradation due to heat or prolonged aeration, if the substance is injected into a metered stream of air by means of a syringe at a controlled speed. If the substance is a volatile liquid, this may be injected conveniently by means of a controlled fluid-feed atomizer. If a solution of a non-volatile liquid or solid in a volatile inert solvent is injected by means of the atomizer, a particulate cloud will be obtained. It is not always possible, however, to obtain a predetermined concentration due to progressive deposition of particles on surfaces.

Another aspect of industrial hygiene air analysis which can be investigated only when known test atmospheres are available is the efficiency of the liquid absorbers which are commonly used as a means of extracting the toxic substance from the air sample. A wide variety of these absorbers have been described in the literature, and some understanding of the factors controlling efficiency of absorption, and the part played by absorber design, is necessary in order to make a rational selection. A vapour or gas in air may be trapped by a liquid in an absorber either by simple solution or by a chemical reaction. When simple solution is involved, the efficiency of absorption, *i.e.*, the fraction of the substance in the air sample which is retained by a single bubbler, is given by the expression

$$E_v = \frac{v}{VK} (1 - e^{-VK/v})$$

where v is the volume of the absorbing liquid, V the volume of the air sample, and K is a constant which is a measure of the volatility of the vapour or gas

from solution. This equation shows that complete efficiency can never be obtained, that it is inversely proportional to the volatility of the vapour or gas from solution, and that it can be improved by keeping the air sample small or the volume of absorbing liquid large. No term is included for the rate of sampling as the derivation of the equation assumes that equilibrium is reached between the concentrations of vapour in the air and in solution; provided that very high speeds are not involved, little advantage in efficiency is to be gained by slower sampling or by the design of the absorber. An increase in the theoretical efficiency shown by the equation can, however, be obtained by using several absorbers in series, but it is very rare that more than two such absorbers are necessary.

A complete absorption of a vapour in a liquid may be possible if a chemical reaction is involved in the retention of the vapour, provided that the time of reaction is short compared with a period of contact between the air and the liquid. Many of the methods commonly applied which make use of this principle, such as the absorption of chlorine in *o*-toluidine solution or of aniline in dilute acid, involve reactions which are so rapid that efficiency is unaffected by the range of sampling speeds usually employed. On the other hand, slow chemical reactions are unsuitable for bubbler absorbers and, if they must be used, one should consider some other method of absorption, such as the exhausted vessel used for nitrous fumes by the diazotization procedure. An example of a reaction of intermediate speed, where efficiency is affected by the design of the absorber, is the absorption of chlorobenzene in formaldehyde-sulphuric acid. Probably the most useful modification of the simple bubbler for this reaction is the inclusion of a sintered glass disc to break up the air stream and reduce the bubble size, but, with the exception of a few special cases of this kind, it may be stated in general terms that the design of a liquid absorber for vapours and gases does not play an important rôle in determining efficiency.

When the atmospheric contaminant exists as a mist, as dust or as fumes, and a weight concentration in air is required, certain important modifications must be made in the design of a liquid absorber. Particulate matter will not be trapped efficiently by bubbling air through a liquid if the size range of the particles is such that their mean-free-path is insufficient to permit a high proportion of collisions with the air-water interface during the life of an air bubble. It is necessary that the dimensions of the absorber and the air sampling speed should be such that the air at the jet approaches the velocity of sound and then impinges on the base of the absorber. Such an absorber is known as an "impinger", and its high efficiency for particles with a diameter of $1\ \mu$ or greater depends on the sudden change in kinetic energy of the particles. This subject is by no means simple, and is made even more complicated when a sample of an insoluble dust is required for a particle size distribution analysis. This problem was discussed in detail at an I.U.P.A.C. Symposium on siliceous dusts, held at Lisbon in 1956.

To sum up, there is an interaction between M.A.C.'s and the analytical methods used for industrial hygiene air analysis. A close collaboration between toxicologists and analysts is desirable, and the selection of analytical methods should be undertaken only by those who are conversant with the special problems involved. The Toxicology and Industrial Hygiene

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Division of the International Union of Pure and Applied Chemistry is composed of such individuals at an international level, and it would welcome the collaboration of other experts. We are very glad to have had this opportunity of associating with the Permanent Committee and International Association on Occupational Health in their deliberations on the establishment of M.A.C.'s of toxic substances in industry.