IRPTC

PREVENTIVE TOXICOLOGY

Collection of Training Materials

Volume II, part II

ED NATIONS ENVIRONMENT PROGRAMME

UNITED NATIONS ENVIRONMENT
PROGRAMME (UNEP)

USSR STATE COMMITTEE FOR
SCIENCE AND TECHNOLOGY
(GKNT)

INTERNATIONAL REGISTER OF
POTENTIALLY TOXIC CHEMICALS
(IRPTC)

USSR COMMISSION FOR UNEP

PREVENTIVE TOXICOLOGY

Collection of Training Materials

Edited by N.F. Izmerov
Corresponding Member,
USSR Academy of Medical Sciences

Volume II
Part II

CENTRE OF INTERNATIONAL PROJECTS, GKNT

Moscow 1984

Collection of instructional materials on preventive toxicology is published by Centre of International Projects, USSR State Committee for Science and Technology under the USSR-UNEP/IRPTC Project "Control of Hazards Posed by Chemicals to Human Health and the Environment" implemented in cooperation with the Research Institute of Industrial Hygiene and Occupational Diseases, USSR Academy of Medical Sciences.

The collection is intended for toxicologists, hygienists and all those responsible for evaluation and control of harmful effects of chemicals to human health and the environment.

Materials of collection may be freely cited and reprinted with a reference to the source. Opinions expressed in instructional materials do not necessarily reflect the official policies of the United Nations Environment Programme. Since the published information was in exact conformity with the data available at the moment of publication, UNEP is not responsible for any errors or omissions or any consequences therefrom.

CONTENTS

Y. PREVENTIVE TOXICOLOGY OF THE COMMUNAL ENVIRONMENT (AIR, WATER, FOOD AND CONSUMER PRODUCTS)

YI. PREVENTIVE TOXICOLOGY OF ECOSYSTEMS

YII. CLINICAL TOXICOLOGY (MEDICAL)

YIII. INFORMATION SYSTEMS ON CHEMICALS; HAZARDS AND RISK ASSESSMENT

Chapter V

PREVENTIVE TOXICOLOGY OF THE COMMUNAL ENVIRONMENT (AIR, WATER, FOOD AND CONSUMER PRODUCTS)

Edited by professor G.N.Krasovsky

TOXICOLOGICAL TESTS FOR THE HYGIENIC RATING OF SUBSTANCES IN WATER

G.N.Krasovsky

In the USSR, to prevent and limit the contamination of water sources with chemical compounds, the sanitary regulations for the protection of bodies of water are based on maximal allowable concentrations (MAC) of substances in water.

These values serve as guidelines in controlling discharges of harmful components into water reservoirs, allowing, on the one hand, to ensure the safety of water supply sources, and thereby of drinking water, and to maintain optimum conditions essential for the economic and domestic water management (recreational, sports, sanitary and household), on the other.

The principles and methods of toxicological tests, used for the substantiation of MACs for new chemicals both in drinking water and in open reservoirs, are essentially the same. Yet, to double-check the hygienic rates applicable to water, the impact of hazardous substances on self-purification (BTC_5 or BTC_{20}, the rate and mineralization pattern of organic substances) must be taken into account.

An integral part of this methodological system is made up of epidemiological studies which are used, when possible, for the purpose of more accurate defining individual ratings and mainly for checking the reliability and improving the elaborated experimental system of establishing MACs. Such a harmonious combination of the two main approaches to the determination of safe concentrations of substances in the environment is in tune with the leading principle of Soviet medicine - the principle of prevention, the observance of which calls for evaluating the toxicity and hazards of substances before their wide-scale introduction into industrial and household use. The practical realization of this methodological premise proved possible owing to the active utilization of the principles of experimental modelling of intoxications on laboratory animals, in combination with the methods of prognostication of the toxicity and hazards posed to man by chemical pollutants in water.

The following stages are envisaged when carrying out these experiments: studies of acute (the establishment of the median lethal dose), sub-acute (specifying the cumulative properties and the toxicodynamics of the compound concerned), chronic (a six-month experiment) and long-term (gonadotoxic, embryotoxic, mutagenic, carcinogenic, allergic and atherosclerotic) effects. In some specific cases the skin-resorptive effect and specific features of transformation of the compounds in water are studied.

Staging the Acute Test and Evaluating its Results

An acute test undertaken within the sanitary-toxicological investigations and aimed at the rating of harmful substances in water reservoirs, allows to obtain information essential for resolving the following tasks.

1. Establishing the toxicity of a tested substance and obtaining the preliminary information on its toxicodynamics.

2. A comparative evaluation of toxicity of several substances with similar physico-chemical properties or conditions of application.

3. Determining the specific, sex and age sensitivity of laboratory animals to the effects of harmful substances.

4. Revealing tentative dose levels in an experiment for studying the cumulative properties of a substance and also for identifying the doses, subject to double-checking in subacute and chronic tests.

5. Substantiating the possibility of abandoning chronic sanitary-toxicological tests for some substances with low threshold values in regard to their organoleptic hazards.

It is advisable to begin the sanitary-toxicological program with an acute test even when the literature provides data on the extreme toxicity of the substance concerned. The results obtained provide an idea about the purity of a sample of tested substance and its chemical stability.

The upper toxicity values, such as DL_{100} (the least dose causing the death of all the test animals) and DL_0 (maximal tolerance dose) are not definite enough.

The experimental determination of DL_{50}, which is the most essential values, is obtained follwing two tests - the tentative and expanded ones.

Once the toxicity of a test substance is unknown, we recommend to begin with acute preliminary tests, aimed at the tentative determination of lethal doses. For this purpose, doses differing by one order of magnitude (for example, 10, 100 and 1,000 mg/kg) are tested on one or two albino mice or rats. For double-checking the severity of the substance toxicity five or six successive doses are tried, each larger than the preceding one by 50-100 per cent; all of them are tested on one animal. Of importance is the fact that the dose found in the course of a preliminary test should occupy an the intermediate position on the scale. The least dose whose injection caused the animal's death, may be regarded as the tentative median lethal dose.

The full-scale test is staged on albino mice and/or albino rats, in which 5-6 doses of the substance are examined. Each selected dose is tested on 6-10 animals.

The number of animals in a group and an interval between the doses largely depend on the method of statistical calculations used further on.

Since all the comparative statistical methods are similar in accuracy and information retrieval potential, preference should be given to the least labour-consuming methods.

If the need arises to test the comparative toxicity of several chemicals with a similar action mechanism, it is advisable to use Leachfield and Wilkoxon's method of analysis (D.J.Finney, 1952). This method provides an objective evaluation of the comparative toxicity of substances when the straight lines of the effect, plotted on a graph, run parallel.

To save the number of test animals (particularly such as rabbits, cats and monkeys) for determining the comparative specific, sex and age sensitivity of laboratory animals to the action of a chemical we recommend the methods of D.J. Finney (1943) and also the one-point method of Van der Waerden (1940).

With the one point one can calculate not only the DL_{50} value but its mean error as well.

More reliable DL_{50} values may be obtained in a small number of animals by the method of 3 or 2 points. This envisages the testing of two doses selected, so that the effect (percentage of dead animals) in one case would be under 50 per cent and in the other over 50 per cent. If the third dose is taken for the test, it should occupy an intermediate position. In this range of doses the dependence of the lethality percentage (Y) on the dose (x) practically always appears as a straight line and is described by the equation: $Y = AX + B$, where A is the angular coefficient, B is the free member (B.M.Shtabsky et al., 1980). Their values are found by the formulas:

$$a = \frac{Y_2 - Y_1}{x_2 - x_1}, \qquad b = \frac{Y - a\,x}{n}$$

, where x_1 and x_2 are the values of the two marginal test doses, Y_1 and Y_2 are the lethality percentages, corresponding to these doses, n is the number of doses tested. Then substituted one by one into the equation ($x = \frac{Y - b}{-a}$) are the y values equal to 50%, 84% and 16% to find x (DL_{50}, DL_{84} and DL_{16}). The values of σ and m are calculated according to the following equations

$$\sigma = \frac{DL_{84} - DL_{16}}{2} \quad \text{and} \quad m = \frac{2}{N},$$

where N is the number of animals in the groups in which at least one animal died or survived.

When using the method of two points, the calculation technique may be simplified as suggested by B.M.Shtabsky and coworkers ((1980) by using the equation:

6300 a

$$\frac{Y - Y_1}{Y_2 - Y_1} = \frac{x - x_1}{x_2 - x_1}$$

To ensure comparable results one should take for the test young sexually mature animals (males or females): mice weighing 16-20 g; rats weighing 16-20 g; rats weighing 150-250 g, gunieapigs weighing 350-500 g; rabbits weighing from 1.5 to 4 kg.

Test substances are introduced into the empty stomach in water solutions, vegetable oil, egg yolk and/or a solution of dimethyl sulphoxide, and also in the form of oil emulsions or starch suspensions; Different doses of the substance should be administered to the animals in solutions of the same concentration and, desirably, in optimum volumes making up 1-1.5% of body weight, i.e. 0.2-0.3 ml for mice; 2-3 ml for rats; 4-6 ml for guinea-pigs and 25-40 ml for rabbits.

In acute tests the administration of substances or their solutions with irritative, as well as strong acid or alkaline properties should be avoided, lest this results in an erroneous conclusion during the comparative evaluation of the toxicity of several substances and in determining specific sensitivity, or the wrong choice of doses for subsequent sanitary-toxicological experiments. This is why in a number of cases it is advisable to administer such substances in 1-2 per cent solution of starch, or in oil.

In some cases one may put to the test neutralized solutions, on condition that the structural part of the molecule determining the substance toxicity is not destroyed or altered in the process of neutralization.

In all the tests the control group should be given equivalent volumes of the solvent.

Occasionally, in acute tests, one has to examine substances of low toxicity which, upon a single administration of the maximal possible doses, do not cause the animals' death. In these cases the following device may be recommended. The maximal allowable concentration of the substance is administered in a volume making up to 5 per cent, and for oil solutions up to 2 per cent of body weight, with an interval of at least 1.5 hours between administrations. By such fractional administration several tens of grams per kilogram body weight may be administered in the course of 6 to 9 hours.

In an acute test the animals should be observed for at least 10-15 days.

In observing the test animals one should pay attention to the animals' behaviour and development of intoxication symptoms. Additional information on a substance cumulative properties after an acute test, may be obtained by applying a method suggested by B.M.Shtabsky (1973).

The acute test may provide primary information on the character of the substance effect.

A more accurate evaluation of the cumulative properties of substances during acute tests may be made with calculation the adverage time of death of the animals ET_{50} (G.N.Krasovsky, 1982).

In some cases, when studying substances of low toxicity, it may be recommended to carry out some biochemical examinations following a single administration to the animals of the maximal possible quantity of the substance. The results may be additionally used for evaluating the toxicity when planning a chronic experiment, when selecting the most sensitive species of laboratory animals.

When the tentative DL_{50} value of a toxicant for which the CL_{50} value (median lethal concentrations upon inhalation of a substance) is known, the following equation may be used (G.N. Krasovsky, 1969);

$$\log DL_{50} = 0.5 \cdot \log CL_{50} + 2.55$$

In some cases the determination of the MAC does not necessitate a chronic experiment, and a study of the acute toxicity will suffice. This conclusion is based on our analysis of accumulated materials on the hygienic rating of harmful substances in water reservoirs. It was established that the ratio of DL_{50} to the maximal non-effective dose of the chronic experiment ($\frac{DL_{50}}{MND}$) for the most of the substances studied, even in cases of extreme variànts, does not exceed 200,000-500, while the ratio of DL_{50} to the threshold concentration in influencing the sanitary condition of the reservoir - 100,000. However, for many substances the ratio of DL_{50} to the threshold concentration, according to the organoleptic criterion, reached one and even several million. This is why it is not necessary to conduct a chronic experiment for low- and medium-cumulative substances in which the DL_{50} ratio to the threshold concentration, according to the organoleptic criterion, reaches 0.5-1 million and higher, while MAC may be recommended at the level of the threshold concentration according to the organoleptic criterion.

Thus, given the observance of a number of conditions for carrying out an acute test, it is possible to obtain comparable data and, therefore, to raise the scientific standards of toxicological examinations for establishing MACs of substances in water.

Cumulative Properties of Substances and Effects on the Body in a Subacute Test

A subacute test makes it possible to obtain information for resolving the following questions:

1. Studying the degree of cumulative properties of a substance.

2. Revealing the functions, organs and systems of the body most vulnerable to the test substance and its toxic action mechanism.

3. Obtaining the data substantiating necessary conditions for chronic sanitary-toxicological experiment (selection of doses, tests).

In some cases when the toxicodynamics of a substance is known, one may carry out, instead of the subacute test, some brief tests for establishing the degree of cumulative properties of a substance. Tests are best carried out on the same animal species for which the chronic experiment is planned.

Functional indicators may also be used to assess the cumulative properties of substances (G.N. Krasovsky et al., 1970) when at least three doses of the substance are tested the difference between them being 5-10-fold (for example, 1/10, 1/50, 1/250 of DL_{50}). If the results of acute tests and calculation of ET_{50} place the substance among compounds with pronounced cumulative properties, the selected doses should be 1/250, 1/1000, 1/5000, etc. The experiment should last not less than 20-30 days. In the animals of all groups, the controls included, after taking the background indicators into account and administering the selected doses of the substance, changes in these indicators are observed on the 5th, 10th, 20th and 30th days of intoxication. It is advisable to carry out each examination 2-4 hours after the substance regular administration.

The test being over, the minimal effective (threshold)dose of the substance is established for the conditions of this subacute test (B.M.Shtabsky, G.N.Krasovsky et al., 1979). For assaying the cumulation by this method, and assessing the degree of hazard the following scale may be used (1) substances with the ratio of the DL_{50} value to the established minimal effective dose of up to 10 should be regarded as low-cumulative; (2) median-cumulative - up to 100; (3) highly-cumulative - up to 1000 and (4) super-cumulative - up to 10,000.

An advantage of this method of evaluating the cumulative properties of a substance is the possibility to select with greater accuracy the test doses for a chronic experiment, and, in particular, a tentative value of the threshold dose. The minimal effective dose which may prove close to the threshold one in a chronic experiment for low- and median-cumulative properties, will be by nearly one order below the threshold dose established in a cumulation test.

When a new substance has to be studied, and its action is practically unknown or hardly known from the literature, the duration of the subacute test should be prolonged to 1.5-2 months, so that more can be learned about the toxicodynamics of the substance by administering high quantities and varying the tests. This makes it easier to select the most sensitive tests for using in a chronic experiment.

The end goal of a chronic experiment is to reveal the maximal non-effective dose of a test substance, with account of which the maximal allowable concentration (MAC) is recommended.

Laboratory animal species most sensitive to the test substance should be used for the experiment. In case of pronounced interspecies differences in the sensitivity of laboratory animals (more than five-fold) or when the animals' biological features prevent or make difficult to utilize tests for studying some specific function (for example, determination of vitamin C in albino rats, study of the conditioned-reflex activity in guinea-pigs and rabbits), it is advisable to carry out a chronic experiment in the laboratory animals belonging to two different species.

When selecting doses it is advisable to use the method of calculated predictions of chronic toxicity parameters.

Depending on the degree of the substance cumulative properties, 3-4 doses (concentrations) should be tested, the difference between them being 5-10-fold.

When using rats a chronic test should last at least 6 months, when using guinea-pigs and rabbits - at least 8 months.

Test methods used in a chronic experiment, should be selected with account of the literary data on the toxicodynamics of the test substance, and also on the subacute test results. It is important to use tests which integrally reflect the body function tests of the conditioned-reflex activity, the body immuno-biological reactivity, and its endocrine function, etc. Tests to study the body functions specifically affected by the test substance should also be applied.

Useful for detecting the minimal effects of pollutants among non-specific indicators are tests of the behaviour reactions and the conditioned-reflex method.

It must be stressed that in most cases only the use of a combination of integral and specific indicators, aimed at the all-round study of the body reactions at different levels of its organization, allows to reliably establish the threshold and subthreshold concentrations (doses) in a chronic toxicological experiment.

Indicators of the body state and of its individual functions are determined at least once a month,with empty stomach in the morning, one hour after the administration of the substance test doses. The frequency of tests depends on the specific features of the function being investigated.

In cases when the chronic experiment is practically over, yet the degree of toxic effect remains unclear, or when changes observed earlier in the process of exposure have disappeared, functional load tests may be recommended. The mostly used functional loads, aimed at studying "constant" indicators, are the galactose tolerance test, the sodium benzoate test, tests with the administration of Bengal rose, vegetotropic substances, studies of the ECG and EEG reactivity curves, etc.

However, the majority of recommended functional loads are nonspecific, inducing functional strain of a number of systems or organs.

A specific load with the test substance proper is free of such shortcomings (G.N.Krasovsky and A.A.Korolev, 1969). Loading with the substance should be used at the end of a chronic experiment on all test animals, exposed to intoxication with various doses of the test substance, including the controls.

This dose of the substance should produce its effect only during the first hours following its administration. The recommended load dose may approximately be from 1/5 to 1/100 of the test substance DL_{50}, depending on its cumulative properties. The effect of the selected load dose should be recorded every hour for 3-4 hours, giving special attention to the degree, stability and direction of the changes in primarily those indicators which proved the most sensitive in the chronic experiment, or whose changes during the preceding period of the experiment were doubtful.

The data obtained in a chronic experiment should be subjected to statistical treatment for establishing the significance of the changes found in the functions under examination.

Far from every experimental material obtained should be subjected to statistical treatment. For example when there is a close approximation of the arithmetic means (M) of the control and of the test, statistical treatment of data is not needed, since the validity of differences between the test and control figures may be assumed beforehand.

By observing these recommendations in chronic experiment, the maximal non-effective dose (MND) can be determined sufficiently accurately. By comparing the MND with threshold effects of the test substance on the organoleptic properties of the water and the sanitary conditions of the reservoir, it is possible to determine the recommended MAC value and the critical indicator of hazardness.

Unlike labour hygiene, concentration rates for the environment are elaborated on the basis of several indicators of hazard, for example, two such indicators are used for drinking water, and three for water reservoirs: the organoleptic, general sanitary, and toxicological indicators. It takes a comparatively short time for the experimental substantiation of the threshold values of the first two indicators (a few days or 1-3 weeks), so that it is not necessary to resort to rapid methods for them. At the same time, they are the ones, which in most cases determine MACs. For example, the ratings for 60 per cent of substances already studied have been established according to the organoleptic criterion of hazard; moreover, for most compounds the gap between the threshold concentrations by the first two indicators and the safe levels by the toxicological indicator of hazard is, as a rule, considerable and may reach from 1,000 to 10,000 times and more.

So the variants of methodological techniques for hygienic rating of substances in water were elaborated with all this in mind, and generalized in a step-by-step rate-setting chart (G.N.Krasovsky, 1977).

The components of a step-by-step establishment of hygienic MACs are a methodological chart and the hazard classification of substances for determining the necessary and sufficient scope of investigations.

Table 4

Substances Classification According to Hazard in a Step-by-Step Establishment of MACs

Order of substance hazard evaluation	Criterion	Class of hazard			
		first (extremely hazardous)	second (highly hazardous)	third (hazardous)	fourth (moderately hazardous)
1	MNC/TC_{org}		1	1-10	10
	MNC/TC_{san}		1	1-10	10
2	MNC, mg/l	0.001	0.001-0.1	0.1	10 10
3	DL_{50}/MND	10^6	10^6-10^5	10^5-10^4	10^4
4	TD_{par}/TD_{gen}	1	1-10	10-100	100

The chart provides for the broad utilization of estimation methods at each step. We regard the results of the prediction of chronic toxicity parameters derived by calculation methods to be an additional safety criterion.

The application of the step-by-step rating allows to slash the time of MACs substantiation by 10 to 20 times for 50-70 per cent substances.

EXPRESS TOXICOLOGICAL TESTS OF WATER POLLUTANTS

Z.I. Zholdakova

At the present time systematic sanitary monitoring of water quality is carried out predominantly with the help of a whole set of chemical methods of testing.

The use of physico-chemical methods if justified when potable water is drawn from subsurface aquifers, particularly through artesian wells which supply water of stable composition (if confined water is not polluted). In this case it is practicable to determine the water's ingredients in spot or periodic tests, while current monitoring will concentrate on those chemical factors which are regulated by the existing potable water quality standards.

However, in certain cases there may occur changes in the confined water's chemical composition and the deterioration of its normally stable quality as a result of unexpected pollution by agricultural chemicals, fertilizers, seepage from the nearby garbage dumps, etc. Such occurrences may call for express methods of identifying the harmful chemical substances polluting the water.

When open bodies of water are used as sources of water supply the health-hazard problem is even more complex. The chemical composition of their water is liable to considerable variation. In addition to such inevitable factors affecting water composition as seasonal and climatic variations, there are a number of man-made causes. According to the findings of a WHO panel of experts (1970), water bodies are being intensively polluted not only in the industrially-developed but also in the developing countries.

The need to monitor the chemical composition of open water bodies stems also from the fact that most of the substances it contains pass through modern water treatment facilities almost unchanged.

It should be pointed out that the existing standards cover only a limited number of chemical ingredients. For example, the US standards provide for the control of 30-40 indices, the WHO standards include a slightly larger number of indices, while under the USSR law 30 substances are subject to regulation. In contrast, the natural chemical components of water alone include between 60 to 90 elements in the periodic table, to say nothing of numerous compounds whose concentrations and combination ratios may differ greatly in every region.

The exact amount of chemicals discharged into the environment is difficult to estimate. For example, according to American data, between 200 to 400 compounds of industrial origin may be discharged into water bodies and find their way into drinking water. It would be wrong, however, to conclude that all tap water is certain to contain hundreds of substances, although the presence of many of them in drinking water is quite likely. For example, 72 organic substances have been found in tap water in five American cities.

Along with the permanent causes of water pollution there exists a danger of sudden drastic water quality changes exemplified by storm run-offs which contain fertilizers and pesticides, or brought about by industrial accidents as a result of highway or railroad accidents in the vicinity of water bodies, as well as a result of accidents on inner waterways which are accompanied by massive discharge of petroleum products, toxic chemicals, etc. Tetraethyl lead may find its way into water bodies as a result of unauthorized and uncontrolled washing of tanks and other containers used for the storage and transportation of gasoline. In summary, there is a danger of both one-time "flash" polluting discharges and permanent inputs of non-natural chemical compounds into water bodies used as sources of potable water. This calls for two types of control: systematic control over substance which as a result of toxicological tests have been shown to permanently reside in water and control over new chemical factors.

The presence of unidentified hazardous factors could be promptly ascertained, though only approximately, with the help of bio-assays. Certain public water-utilities have tried to control tap water quality using assays of fish, other aquatic life and plants placed in aquariums through which tap water is continuously pumped. At the same time biological control methods have a number of drawbacks. For example, the use of just one type of bio-assay does not assure sufficient reliability of control, because the sensitivity of aquatic life to different groups of substances differs from species to species and from class to class.

Water quality control based on the lethal effect on aquatic life is not reliable enough, since concentrations toxic to it frequently and to a considerable extent exceed the safety levels for man.

In addition, low-intensity chemical factors bring about the impairment of aquatic life only after a certain period of time, which rules out the use of biological testing as an express method of water quality control. Bio-assay methods cannot be used to control all water quality indices, for example its organoleptic properties. The following data may be used to illustrate these observations. As a rule, lethal concentrations for fish (V.V. Metelev et al.) and harmless long-term levels for man do not coincide. A number of substances (nitrites, calcium salts, lead, etc.) kill fish in concentrations which are 100 to 10,000 times greater than the hygienic MACs, whereas it takes a concentration of cyanides equal to one-fiftieth of the MAC to produce the same effect. This means that in a number of cases the discovery of a lethal effect on aquatic life will be made only when the pollution has already reached a level hazardous to man. In other cases, the lethal effect on aquatic life may result in an unduly pessimistic assessment.

With a view to elucidating the possibility of using lower animal species as targets for biological testing in predictions of toxicity to higher animal species and man, G.N. Krasovsky et al. (1973) carried out a comparison of lethal amounts for different animal classes and species. The comparison has shown that there is no mathematical correspondence between chemical toxicities for man and bacteria (aquatic saprophytes) in terms of BOD- the correlation coefficient is 0.15. The values of DL_{50} for rats and CL_{50} for fish have been shown to correlate but weakly: the correlation coefficient is 0.49 ±0.68. The correlation coefficient for rats and Daphnia, obtained on the basis of the toxicities of 49 substances, was 0.525 ±0.125. It is characteristic that certain substances were highly toxic for aquatic life and little toxic for mammals, whereas vegetotrophic compounds, certain narcotics, and other substances highly toxic for man and higher animal species, produced practically no effect on fish and Daphnia. The role of the stage of philogenetic development in sensitivity to toxic substances is further proved by the following series of correlation coefficients between toxicity for rats and those for a group of other vertebrates - fish, amphibia, birds, cats and man: 0.490; 0.619; 0.821; 0.905; 0.861. A higher degree of correlation might be obtained in the investigations of individual classes of substances taking into account the mechanisms of their action as well as in the comparisons of the data obtained under standard conditions. For example, H. Könemann found the CL_{50} for the guppy (Poecilia reticulata) under standard conditions - stable temperature, hardness, salt composition, etc. - of water quality. We have compared Könemann's data with a minimum ineffective dose (MED), a threshold dose (TD) and the DL_{50} values determined by us on the basis of the standard methodology. The analysis of toxic effects of 17 chlorine derivatives of benzene on white rats and fish has produced the following dependable equations:

$$\lg DL_{50} = 0.21 \lg LC_{50\ p} + 3.06 \quad r = 0.85; \ s = 0.18 \qquad (1)$$

$$\lg MED = 0.59 \lg LC_{50\ p} + 3.07 \quad r = 0.74; \ s = 0.77 \qquad (2)$$

$$\lg TD = 0.62 \lg LC_{50\ p} - 2.31 \quad r = 0.79; \ s = 0.74 \qquad (3)$$

The second series of 15 substances included xylol isomers and chlorine derivatives of toluene, as well as halogen-substituted aliphatic compounds, including esters, in other words it was structurally inhomogeneous. The equations in this group do not have the necessary level of confidence:

$$\lg DL_{50} = 0.17 \lg LC_{50\ p} + 2.79 \quad r = 0.47 \quad s = 0.54 \qquad (4)$$

$$\lg MED = 0.37 \lg LC_{50\ p} - 2.79 \quad r = 0.60 \quad s = 0.70 \qquad (5)$$

$$\lg TD = 0.15 \lg LC_{50\ p} - 0.91 \quad r = 0.35 \quad s = 0.68 \qquad (6)$$

The aggregation of the substances in the first and the second groups into one series did not produce a sufficiently high level of confidence either.

It follows that significant correlations between toxicities for aquatic life and mammals can be obtained for structurally close compounds. However, it is seen from the above equations that the toxicological parameters may differ by 2-3 orders of magnitude.

The conclusion is that attempts to use just one species of aquatic life, one tissue culture or one species of microorganism (e.g. B.thyphy murium) for bio-assays are hardly justified, while a system of bio-assays taking into account its sensitivity to different classes of substances would assure a much more reliable biological control.

In summary, the existing biological methods permit integral assessments of hazardous changes in the chemical composition of water, while chemical analytical methods are more reliable for the identification of individual pollutants. However, health-oriented interpretation of chemical measurements can be based only on the existing maximum allowable concentrations (MAC) for man.

It takes several skilled toxicologists two or three years to come up with scientifically substantiated maximum allowable concentrations. That is why, when there is no time for a complete health-oriented toxicological assessment of a substance, one needs a set of prompt and economical methods of predicting its toxicity and safe levels for the biological and physical objects of the environment. The most economical solution is the adaptation of other countries' official safe levels to the objectives sought by one's own country. If the two countries use identical basic principles and methodologies for the elaboration of safe levels, they may be adopted without any modifications. The research carried out within the CMEA framework is a good example of such common use of data. At the initial stage the specialists from the CMEA member-states agreed on common methodology and requirements to be met by chemical toxicity studies and the elaboration of MACs for aquatic life and plants. This was followed by the practical use of the MACs developed by some CMEA members by other member-states in their sanitary legislation. A similar example is provided by the WHO standard of potable water quality which was arrived at after the analysis and generalization of several countries' experience and the final discussion and adoption of the standardized values by a panel of experts.

It has been shown that the indices of approximately 70 substances figuring in the US drinking water standards can be used to improve the corresponding USSR standard. Similarly, a number of indices produced by Holland and Norway can be used for the purpose. This goes to illustrate the point in certain cases safe levels produced by one country can be transfered into the legislation of another country without any modifications. However, it is better to adapt these standards to the national legislation in the light of accumulated experience. Investigations carried out in Professor G.N. Krasovsky's laboratory have shown that even in cases when the methods used to produce safe levels do not quite coincide, it is possible to use correlation-regression analysis to determine a pattern which governs possible adaptations. It has been shown, for example, that the most reliable equations are produced on the basis of comparisons of toxicity data between groups of structurally similar compounds. As a result, subsequent studies were aimed at correlations between toxicity indices obtained in the elaboration of the MACs of chemical pollutants in atmospheric air, the air of the working zone and open water bodies, along with West German and US MACs, for the substances making up two sufficiently studied groups: aromatic hydrocarbons and fat-containing amines - a total of 36 substances. In a number of equations it has proved to be possible to use West German MACs for the air of the working zone. For example, the following equations were obtained for fat-containing amines:

$$\lg DL_{50} = 2.695 + 0.339 \lg \text{West German MAC} \qquad (7)$$

$$r = 0.881 \qquad p \quad 0.01$$

$$\lg \frac{DL_{50}}{TD} = 2.62 + 0.605 \times \lg \text{West German MAC} \qquad (8)$$

$$r = 0.549 \qquad (p = 0.01)$$

In a majority of cases the correlation coefficients calculated for the totality of the two groups of substance did not reflect their actual inter-dependence within each group, which seems to be due to the different toxic effect mechanisms ob benzene and amines.

The prediction of MACs in water on the basis of the standards established for other environmental objects presents a particular interest, since it is based on materials which have the greatest relevance to health. For example, formulas based on MACs of the air of the working zone make it possible to calculate such chronic toxicity parameters as the overall toxic effect and the long-term (mutagenic, gonado- and embryotoxic) effects. This can be illustrated by the following equations:

$$\lg MED = 0.60 \lg MAC_{wz} - 1.31 \qquad (9)$$

$n = 133 \quad r = 0.55 \pm 0.06 \quad t = 7.6$

$$\lg TD = 0.74 \lg MAC_{wz} - 0.37 \qquad (10)$$

$n = 122 \quad r = 0.59 \pm 0.073 \quad t = 8.1$

where:

MAC_{wz} - is the MAC of substances in the air of the working zone.

Modern toxicology uses mathematical computations based on the biological and physico-chemical properties of substances. Since the toxicity and the reliability of predicted values are not one and the same thing, their choice should be dictated by the objectives pursued. For example, it has been shown by Lyublina et al., G.N. Krasovsky et al., and A.I. Zholdakova and others that mathematical correlations between simple physico-chemical constants and the toxicity of substances is not sufficiently trustworthy, since the constants do not reflect the characteristic features of the mechanisms of intake and the substance's action upon its entry into the digestive tract. Molecular constants seem to be the most acceptable, since they characterize the structural peculiarities of chemical compounds.

The search for correlations between the magnitude of toxic effect and the chemical structure is substantiated and logical since it is precisely a combination of several molecular parameters and their interaction that largely determine the substances' mechanism of action and the degree of toxicity.

Shitskova et al., 1973, succeeded in using such physico-chemical constants as Taft's coefficient, the dipole moment, the ionization potential and polarizability in the predictions of MACs in winter. However, all equations thus obtained were derived on the assumption of the correlation between the MACs in one of the constants under study. We can hardly agree with the correctness and credibility of this method of derivation, since it is by far not in all cases that toxicity is determined by just one physico-chemical factor.

Correlating biological activity with a group of molecular constants suggested by Hansch (1976) seems more reliable.

Another approach to the prediction of the toxicity and hazard of chemical pollutants of water consists in the combined use of a short-term toxicological experiment and a computational procedure based on equations.

Several equations have been suggested to calculate the MED and the TD of substances on the basis of DL_{50}:

$$\lg MED = 0.90 \times \lg DL_{50} - 3.60 \tag{11}$$

$n = 260 \qquad r = 0.52$

$$\lg TD = 0.99 \times \lg DL_{50} - 2.83 \tag{12}$$

$n = 236 \qquad r = 0.55$

$$\lg MED = 0.886 \times \lg DL_{50} - 3.602 \tag{13}$$

$n = 30 \qquad r = 0.973$

However, the equations are applicable only to moderately cumulative substances, since they take into account only one of the chronic toxicity components - the value of acute toxicity.

The second component which greatly influences the MED of the chronic experiment - the cumulative effect of substances - is not included in the equations. This makes it obvious that the equations predicting the MED on the basis of DL_{50} cannot be used directly, solely on the basis of the results of acute experiments. The equations' accuracy and reliability may be greatly heightened by an additional experiment consisting in repeating the administration of a substance with a view to identifying its cumulative effect, accompanied by determination of its adjustment coefficients whose magnitude is proportionate to the magnitude of the cumulative effect. It must be noted, however, that the time required for the computation of the corresponding MED estimate increases to 1-4 months.

Used for assessing cumulative effects of the substance directly on the basis of the acute experiment data was the average extinction time of animals (aquatic life) suggested by B.M. Shtabsky as a parameter characterizing the cumulative effect. A method of computational and graphical determination of average extinction times ET_{50} corresponding to DL_{50} was elaborated and a correlation between this index and the $\frac{DL_{50}}{MED}$ assessment of cumulative effects (G.N. Krasovsky et al., 1976) was found.

Our data show that intercomparisons of different forms of correlation is productive in few cases only, since making a model more complex does not always result in a higher confidence level. Our investigations have confirmed the assertion made by E.I.Lyublina (1979) to the effect that as far as toxicity parameters are concerned (DL_{50}, MED, etc.) logarithmic dependence is preferable, since the simple mathematical averaging of these parameters results in greater errors in the case of the most toxic substances which are also the most relevant in the discussion of health problems.

It should be pointed out. however, that the indiscriminate use of even the most refined mathematical methods may still result in errors, because the logical links between the parameters under study should remain the overriding principle in the development of new formulas.

An example of such indiscriminate use of mathematical models can be provided by the search for the correlation between the smell and the toxicity of substances, the smell and the molecular mass, as well as by attempts to compute toxicological parameters on the basis of MACs in water which are normally based on one of the following three indices of harmfulness: the organoleptic, sanitary and toxicological.

During the last few years different authors suggested 400 mathematical equations to be used to compute a variety of toxicohygienic parameters and the number is continuing to grow.
With a view to establishing a definite order in the use of computational methods we have developed the following guiding principles:

1. The principle of logic, according to which those prediction methods are to be given priority, is based on indices which are linked by direct, logical and pathogenic dependence.
2. The principle of comprehensiveness in the use of computational equations according to which a computation of a chronic toxicity parameter should be based on the use

of several equations (not less than 2 or 3) including different constants and indices.

3. The principle of preference which means that whenever there is extensive information on a substance and a possibility of calculating its chronic toxicity parameters on the basis of many constants and indices, the ones to be preferred are those which are more reliable and relevant to health, in the following order of preference: physico-chemical constants - toxicometric indices (DL_{50}, CL_{50}, ET_{50}) and MACs in other environments. Equations for individual classes of chemical compounds are to be given preference.
4. The principle of a stage-by-stage approach according to which the reliability of prediction increases as new information on the subject is amassed in the following sequence: physico-chemical constants - cumulative effects - the results of subacute experiments.
5. The principle of limitation which means that the levels of substances with possible long-term effects safe for man cannot be deduced from indices describing general toxic effects. Predictions of safe levels of such substances should be based on equations using MACs in other environmental objects or threshold doses found in the course of express experiments taking long-term effects into account.
6. The principle of optimization which means: if the results obtained with the help of three different equations are close to one another, the smallest one is to

be used; if two of the values obtained are too divergent, none of them can be used and the prediction experiment is to be continued until 2 or 3 convergent values are obtained.

7. The principle of correspondence which means that the predicted value's degree of precision should correspond to its purpose. For example, in a chronic experiment doses are to be selected on the basis of the equations with limited precision and reliability, whereas the prediction of levels safe for man should be based only on the use of high-precision methods.

The use of express methods of health-oriented regulation is both necessary and possible since it is based on a solid scientific foundation.

The problem of the prompt development of health standards should not be reduced to the prediction of time-weighted averages. The use of the latter is justified in certain instances only: at initial research and development stages, during feasibility studies, prototype tests, etc., with a view to determining the required sensitivity of the analytical methods to water quality control objectives or to replacing process substances by less hazardous ones.

A generalized scheme of stage-by-stage regulation of substances in water using several methodologies has been suggested (G.N. Krasovsky, 1977).

REFERENCES

1. Ltublina E.I., Mikheev M.I., Dvorkin E.A., Sidorkin G.I., Lisman M.V. - O vozmozhnosti rascheta OBUV organicheskikh veshchestv po dostupnym fiziko-khimicheskim konstantam i parametram ostroy toxichnosti. In collected papers: Nekotoriye voprosy exp. prom. tox., Moscow, Minzdrav RSFSR, 1977, pp 28-45.

2. Krasovsky G.N., Zholdakova Z.I., Yegorova N.A. - Metodicheskiye osnovy uskorennogo gigiyenicheskogo normirovaniya vrednikh veshchestv v vode. In collected papers: Problema porogovosti v toxikologii, Moscow, Minzdrav SSSR publishers, 1979, pp 27-50.

3. Zholdakova Z.I. - Collected Papers: Aktualniye voprosy gigiyenicheskoy toxicologii (First scientific and practical conference 10-12 April 1972), Moscow, 1972, pp 38-39.

4. Shitskova A.P., Yelizarova O.N., Pavlenko S.M., Yegorov U.L., Plitman S.I., Ryazanova R.A., Nosikova V.V., - Gigiyena i Sanitariya Journal, 1973, No.5, pp 30-34.

5. Hansch C. - J. Med. Chem., vol. 19, pp 1-6.

6. Shtabsky B.M. Gigiyena truda i profzabolevaniya journal, 1974, I, pp 23-28.

7. Krasovsky G.N., Yegorova N.A., Zholdakova Z.I., Borisov A.I., Prokopenkova E.A., Khitrova N.I., - Express experimentalny metod prognozirovaniya parametrov khronicheskoi toxichnosti po pokazatelyu ET_{50}. In collected papers: Aktualniye voprosy ekologicheskoi toxikologii, Minzdrav RSFSR, Ivanovo, 1976, pp 44-46.

8. Sidorov K.K., Shcherbakov B.D., Tepikina A.I. - Vybor matematicheskikh modelei dlya rascheta parametrov toxikimetrii

REFERENCES (continued)

s tselyu obosnovaniya OBUV vrednykh veshchestv v objektakh vneshnei sredy, Ibid., pp 64-67.

9. Murzakayev F.G., Maximov G.G., Khakimov B.V. - Gigiyena i sanitariya journal, 1980, No.6, pp 56-59.

10. Krasovsky G.N., Shagan S.A., Vitvitskaya B.K. et al. In: Vsesoyuzny simpozium "Primineniye matematicheskikh metodov otsenki i prognosirovaniya realnoi opasnosti nakopleniya pestisidov vo vneshney srede i organisme", Proceedings of the 1st national symposium, Kiev, 1971, pp 47-53.

11. Krasovsky G.N. - In: Voprosy okhrany okruzhayushchei sredy, Perm, 1977, pp 19-22.

12. Krasovsky G.N., Sutokskaya I.V. - Gigiyena okruzhayushchei sredy (Express informatsiya), 1977, No.10, p 24.

Methodological Aspects of Toxicological Research into Desalinated Water Quality Evaluation

Yu.A.Rakhmanin

Desalination may involve a change in water's state of aggregation or do without it.

Processes involving a change in water's state of aggregation.

This group of methods (freezing and especially distillation) is characterized by profound structural changes of water, including alteration of its gas, macroelement, microelement, organic and microorganism content.

Distillation. The sum total of transformations to which they are subjected makes distillates produced by industrial desalination plants the poorest sort of fresh water from the hygiene point of view. It has been shown that completely salt-free and weakly mineralized (up to 100 mg/l) desalinated water is physiologically unwholesome in its salt content; its consumption results in a deregulation of the water-salt balance, its other negative effects including increased excretion of water, so-called "leaching" or certain salts from the organism (primarily electrolytes - Na, K, Cl and Ca), excessive strain on the water-salt homeostasis regulatory systems (changes in electrolyte concentrations in the blood serum, water-space ratio and the pituitary -adrenal function), destructive changes in the gastro-intestinal mucous membrane, changes in the secretory function and the muscular tension of the stomach, as well as lower capacity to quench a thirst. (18, 14, 7, 1, 16).

Absence or low levels of hardness salts, primarily calcium, in desalinated water, have the effect of changing the phosphorus-calcium exchange towards the reduction of bone tissue mineral saturation, depletion of calcium, reduced activity of alkali phosphatase in blood serum and alteration of the thyroid functional state. According to M.F. Stiff (1971), the reduction of bicarbonate hardness of water may heighten the toxic effect of copper and some other elements. The addition of 1.5 mg. equiv/l of calcium to desalinated water palliates the changes. The addition of 1.5 mg.equiv/l of calcium accompanied by bringing water alkalinity to 0.5 mg. equiv/l (HCO_3 - 30 mg/l) improves desalinated water's taste, sharply reduces its corrosivity and increases quality stability.

Distillation largely removes most of the microelements from water. At the same time, distilled water may have elevated contents of certain microelements (bromine, iron, copper, nickel and manganese). Studies have shown that bromine may produce significant biological effects: it can affect the central nervous system, enzyme systems, blood composition and a number of important functions of the organism.

An important characteristic of the distillation process is that it puts up a barrier in the way of organic pollutants. Depending on the quality of crude water, oxydizability may be reduced by a factor of 3 to 10. Cancerogenic substances are completely removed by high-temperature distillation. On the other hand, the so-called "light" organic substances which have boiling points below 110°C, build up in it in concentrations higher than those in crude water - an example is pollution with phenols whose concentrations in distilled water may be a factor 1.5 or 2 higher than in crude water (15).

It was shown that organic impurities of distilled water were mostly made up of methanol-soluble substances (≈ 56 per cent), including oxygen-containing ones, many of which are natural components of sea water (plancton degradation products, vital activity products of higher marine vegetation and animals). The second group (≲ 6 per cent) comprised pollutants which had entered sea water with industrial and domestic sewage (for example, detergents). Substances of groups III and IV were present in insignificant amounts (between 1 and 2 per cent) and comprised mainly oxygen-containing polar compounds. Group VII was represented by phenols (≲ 6 per cent) and Group VIII (≈ 28 per cent) - by neutral compounds mostly organic substances of oil origin (3).

Among other major sources of pollution of the finished product are reagents and polymers used as technological or structural materials (water-repelling heat-transfer agent piping of heat exchangers, anti-corrosion linings and anti-scaling compounds).

Freeze desalination

This group of processes makes it possible to obtain desalinated water of any level of mineralization, depending on the extent of ice washing-off. The efficiency of desalination also depends on the ice crystallization rate which determines the size and quality (purity) of ice crystals.

The preliminary data obtained on the biological properties of desalinated water of different structure (6), along with numerous data reported in literature on the favourable effect of thaw water on a living organism (4) provide evidence of the advantages offered by freeze desalination in this respect.

A characteristic feature of the freeze-desalination methods is that they tend to pollute desalinated water with cooling agents. Their residual concentrations in desalinated water must not be more than 0.2 mg/l for butilene and 10 mg/l for freon-12 and freon-22.

Membrane and Ion-Exchange Processes

This group of methods is characterized by partial desalination, with the exception of ion exchange which may be used in industry for deep desalination of water. Their use does not involve any change in water's state of aggregation.

Electrodialysis. Desalination efficiency of the method is directly proportionate to the current density and the duration of the desalination cycle. It also depends on the membranes' selectivity, the degree of mineralization and the composition of crude water.

Electrodialysis sharply reduces (by approximately one half) the content of most common organic impurities - petroleum products, cancerogenic and surface-active substances, and removes 30-35 per cent of phenols.

Reverse osmosis. Desalination efficiency of reverse osmosis is directly proportionate to the membranes selectivity, while plant productivity is inversely proportionate to it.

A specific feature of this group of methods is not only the high desalination efficiency but also the high (much higher than in the case of electrodialysis) degree of removal of organic impurities and microorganisms: even with membranes selectivity of 70 per cent with respect to Na, Cl, reverse osmosis removes 52, 80 and 70 per cent of petroleum products, cancerogenic and surface-acting, substances, respectively.

Membrane methods are not efficient enough in removing such biologically active microelements as bromine and boron which may have a number of negative effects: general toxic (affecting hydrocarbon metabolism and enzyme systems), embryotoxic, gonadotoxic and terratogenic effects. In spite of the fact that, with initial bromine and boron concentrations in sea water of 60 and 4.5 mg/l respectively efficiency, of their holdback by electrodialysis is 97 and 60 per cent respectively, the two elements' residual concentrations in desalinated water (1-2 mg/l) are still much higher than e.g. Soviet hygienic standards for bromine and boron - 0.2 and 0.5 mg/l.

Since electrodialysis and reverse osmosis installations commonly use polymers as impermeable membranes, underlying and supporting materials and drainages, individual organic substances washed out of these materials may find their way into desalinated water.

An investigation of most common polymer materials (ionite, membranes, acetylcellulose, nylon and polyamid films, polyvinyl chlorid plastic myplast, paronite, etc.) has shown that at the initial stage of the desalination plants operation insufficient washing of filtering and structural materials, as well as accelerated destruction of certain polymer structural materials after prolonged use may introduce certain chemicals as well as unidentified organic matter into desalinated water. This may negatively effect organoleptic and biological properties of desalinated water.

This makes it necessary, first, to wash unpolymerized organic substances off polymer materials, and, secondly, to control their residual content in desalinated water. According to some data obtained in the USSR, this latter should not be in excess (depending on the polymer materials used) of 0.1 mg/l for styrene, 0.01 mg/l for epichlorohydrin in the case of electrodialyses, and of 0.4 mg/l for dimethylacetamide, 0.01 mg/l for formaldehyde, 1 mg/l for phthalic acid and 0.001 for phenol in the case of reverse osmosis.

Ion exchange. The method can be used for selective removal or replacement of individual salt ions (softening, calcium, enrichment).

It has been established that the completeness of the exchange increases with valency or with the increase of atomic number. Ion exchange desalination is notable for its high efficiency, of iron and nitrates removal.

A serious drawback of Na- cation water softening is the high alkalinity of water. In vivo and in vitro studies (2) have shown that elevated alkalinity of drinking water deregulates the acidalkali balance and the water-salt exchange. As a consequence, bicarbonate content of water should not be in excess of 6.5 mg. equiv/l (400 mg/l), and sodium content = not in excess of 200 mg/l. Water alkalinity may be reduced with the help of lime pretreatment, as well as combined or parallel H- and Na-cation exchange.

It has been established that ionites normally contain unpolymerized matter and products of accompanying reactions and, in the case of polymer "ageing" - products of their destruction: phenol, styrene, formaldehyde, etc. As a consequence, initial and prolonged use of ion-exchange resins (average life time of ionites is between 1 and 5 years) may result in a deterioration of water's organoleptic properties (smell, taste) and increased oxidability. Laboratory animals have been shown to be negatively affected by water desalinated with insufficiently clean ionites. (13, 5).

Comparisons of different desalination methods should be based on all-round evaluations of reagents at the stage of laboratory assessment of industrial prototypes which include as necessary stage the study of the reactant's possible influence on water's biological properties with a view to determining the nature and degree of their potential hazard for aquatic organisms (including microflora) and warm-blooded animals.

In such studies it is useful to take into account the above specific properties of water desalinated by different methods and the possible transformations of reactants during the desalination process. This can be done on scaled-down models of desalination plants. Toxicological assessment of reactants are carried out on warm-blooded animals, normally in acute, subacute and chronic experiments (lasting 10-12 months) with account taken, depending on the biological properties, of possible long-term effects: gonadotoxic, embryotoxic, mutagenic, cancerogenic and allergenic ones.

Health assessments of structural and technological materials, mainly polymers, are also based on the above considerations. At the same time they must include the whole range of both known and unidentified substances which may be leached from polymers after their degradation by prolonged use or as residues of unpolymerized initial products. This calls for additional investigations of levels and migration rates of individual organic substances and combinations of them passing from polymers to aqueous environments both under extraction conditions and in the course of model experiments. Total carbon, polar and unpolar hydrocarbon content, permanganate and bichromatic oxidizability, rates of biochemical and chemical oxygen uptake are among major direct and indirect integral indicators of water pollution by organic substances.

It is believed (11) that health assessments of structural and technological materials are primarily designed to determine and regulate permissible levels of migration of hazardous chemical substances from them into water environment. Bearing in mind the variety of factors which may influence the levels and rates of migration of chemical substances from structural and technological materials into water (specific area, time of contact with water, temperature, mineral content, pH, washing time, etc.), prompt, accurate and comprehensive health assessments of these materials can be obtained with the help of mathematical modelling of multifactor experiments.

The above characteristics of desalination technologies and quality of desalinated water have led to a need to work out additional criteria, indexes and standards of water quality.

According to the national, European and international standards the traditional indexes of fresh water quality include first of all salt, microelement and microbial composition, while existing standards for potable water quality are primarily based on the higher (maximum permissible) limits of the indexes which are sought to be regulated. It is these main indexes whose choice is dictated by the requirements of the existing standards that underlie the universally recognized criteria of potable water quality: good organoleptic properties, harmless chemical composition and epidemiological safety.

In assessments of desalinated water quality, great significance is also attached to such indexes as organic matter content, the structure of water molecules, deuterium content and certain characteristics of the microbial composition of salt water (including sea and ocean water).

These indexes, along with the preceding group of ones, call for the use of such additional quality criteria (16) as physiological wholesomeness and stable quality.

So the quality of desalinated potable water not only must answer to a specific standard used by a country (international, European or national as the case may be), but also meet a number of other hygiene requirements which are determined by the specific features of technologies used for the desalination of salt and brackish waters.

- minimum necessary level of mineralization - 100 mg/l,
- optimal mineralization limits of:
- chloride-sulphate waters - from 200 to 400 mg/l,
- hydrocarbonate waters - from 250 to 500 mg/l,
- maximum permissible alkalinity of water - 6.5 mg.equiv/l,
- minimum necessary alkalinity of water - 0.5 mg.equiv/l,
- minimum necessary water hardness - 1.5 mg.equiv/l,
- minimum calcium content - 30 mg/l,

- boron content - not in excess of 0.5 mg/l,
- bromine content - not in excess of 0.2 mg/l,
- temperature of water supplied to the consumer - not higher than 25°C,
- sodium content - not in excess of 200 mg/l.

Whenever it is necessary to control the content of a number of other microelements in desalinated potable water,one may be guided by their maximum permissible concentrations used in the USSR (see Table 1).

All the above-mentioned considerations helped to reveal the following basic peculiarities of the biological activity of desalinated drinking water:

- While controlling the macro- and microelement composition it is necessary to conduct an input-output analysis in order to determine the relative role of the studied elements entering the organism with water and food and then excreted. Besides, the difference ratio between the studied levels of exposure should not exceed a factor of two and the test period should last at least 10-12 months. While planning a test it is reasonable to apply a systems approach and to model different "susceptibility" states (atherosclerotic cardiosclerosis, myocardial infarction, renal insufficiency, etc.) in order to verify the mechanism of revealed biological effects;

- While assessing the impact of reagents and different chemical substances contained in the original water on the

Table 1

Maximum Permissible Concentrations (MPCs) of Selected Chemical Elements in Water Bodies

Element	Symbol	Threshold concentration (mg/l) affecting:		Subthreshold toxicological concentration (mg/l)	MPC (mg/l)
		organoleptic properties	water body' sanitary regime		
Barium	Ba^{2+}	4	10	50	4
Berillium	Be^{2+}	-	0.01	0.0002	0.0002
Tungsten	W^{6+}	6	0.1	I	0.1
Cobalt	Co^{2+}	1000	I	3	I
Molybdenum	Mo^{2+}	10	5	0.5	0.5
Nickel	Ni^{2+}	50	0.1	I	0.1
Silver	Ag	-	-	0.05	0.05
Strontium	Sr^{2+}	12	>400	7	7
Antomony	Sb^{3+}	0.6	0.5	0.05	0.05
	Sb^{6+}	0.6	0.5	0.05	0.05
Tellurium -	Te^{2+}	-	-	0.01	0.01
	Te^{4+}	1.5	0.1	20	0.1
Titanium	Ti^{4+}	4.5	0.1	20	0.1

Source: PDK vrednykh veschchestv v vode vodoyomov, MZ SSSR, 1973 (MPCs of harmful substances in water bodies, the USSR Ministry of Health, 1973).

quality of desalinated water, it is necessary to take into account a possibility of a radical change in their toxicodynamic properties as a result of a chemical transformation or a fractional division (especially in case of high-temperature distillation). For this purpose tests must be conducted in conditions close to the technological ones;

- In all tests with polycomponent compounds (saline composition, polymer materials, complex reagents, etc.) it is necessary to take into account the complex effect of mixtures of chemical substances (elements) on the organism (for instance, cobalt and selenium reduce the amount of magnesium and copper in the myocardium; magnesium provides protection from the toxicity of lithium on the one hand while its shortage, on the other, encourages the precipitation of calcium in the arteries; calcium blocks the absorption of cadmium and lead, etc.). In this connection it is reasonably to simultaneously use both specific and integral biological tests, especially general and specific functional loads;

- Whenever a positive result is obtained after testing a technology of water desalination, it is by all means necessary to keep on checking in future the health of the public who uses this water as potable water.

References

1. Bokina A.I., Rakhmanin Yu.A., Plunin V.P. Vestnik AMN SSR, Moscow, 1975, N.3, 41-46.
2. Budeev I.A. - Collected Papers "Problemy okhrany okruzhayushchei sredy v svete resheniy XXIV s'ezda KPSS", Barnaul, 1977, 78-81.
3. Yegorov A.I., Rakhmanin Yu.A., Ivleva G.A. - Trudy Instituta "VODGEO" "Nauchniye issledovaniya v oblasti vodosnabzheniya", Moscow, 1977, vyp. 66, 42-44.
4. Lastkov O.A. - "Gigiyena i Sanitariya" journal, Moscow, 1977, N. 1, 73-76.
5. Omelyanets N.I., Panasenko G.I., Vlasova L.P. - Collected papers "Gigiyena naselennykh mest", Kiev, 1971, 75-77.
6. Rakhmanin Yu.A., Plugin V.P., Kutepov E.N. - Collected papers "Gigiyenichiskiye aspecty okhrany okruzhayushchey sredy". Sysin Institute of General and Communal Hygiene of the USSR AMS, Moscow, 1974, 69-74.
7. Rakhmanin Yu.A., Bokina A.I., Plugin V.P. et al. - "Gigiyena i sanitariya" Journal, Moscow, 1975, N.7, 16-22.
8. Sidorenko G.I., Shtannikov Ye.V., Rozhnov G.I. et al. - "Gigiyena i Sanitariya" Journal, Moscow, 1978, N.2, 11-15.
9. Sidorenko G.I., Rakhmanin Yu.A., Rozhnov G.I. et al. - "Gigiyena i Sanitariya" Journal, Moscow, N. 11, 14-20.

10. Samoilov O.Ya. Struktura vodnykh rastvorov elektrolitov i gidratatsiya ionov, Moscow, 1957.

11. Sheftel V.O., Katayeva S.Ye. - Migratsiya vrednykh khimicheskikh veshchestv iz polimernykh materialov, Moscow, Khimiya Publishers, 1978, 168 p.

12. Shpakovich V.M. - Kontsentrirovaniye mikroorganizmov, toksikonov iz vody i eye obezzarazhivaniye v protsessakh umyagcheniya i demineralizatsii na ionitakh. Ph.D. Thesis, Moscow, 1975.

13. Shtannikov Ye.V. - Ionnoobmennyye polimery i ikh ispolzovaniye v probleme gigiyeny vody i vodosnabzheniya". Ph.D. Thesis, 1964, Leningrad.

14. Elpiner L.I., Bokina A.I., Shafirov Yu.B. - "Gigiyena i Sanitariya" Journal, Moscow, 1969, N.6, 22-26.

15. Hakuta Toshikatsu, Negishi Akita et al. - Bull. Soc., Sea Water Sci., Jap., 1976, 29, N. 6,. 255-260.

16. Sidorenko G.I., Rakhmanin U.A. -"Proceedings of the 6th International Symposium - Fresh Water from the Sea", 1978, vol.1, 65-74.

17. Harold R. Shipman - Water Desalination. Public Utilities Department PUN 9. Central Projects Staff, 1973, 11 p.

18. Williams A.W. - "Gut", 1963, 4, 1.

TOXICOLOGICAL CHARACTERIZATION OF WATER QUALITY RESULTING FROM ITS THREATMENT AT WATERWORKS

N.Ya.Mikhailovsky

In recent years an ever greater attention of investigators has been drawn to the problem of studying the influence of water quality on public health manifesting itself as the so-called long-term chronic effects - i.e. the growth of oncological and genetic morbidity. A number of investigators believe that the current difference in the incidence of cancer in different regions, countries and even within one country can be associated with the etiological factors of the environment, i.e. chemical carcinogenic substances of natural and technogenic origin (Higginson, Callum, 1976; Heath, 1978).

The chemical substances to which the increasing incidence of various forms of malignant neoplasms is attributed include a vast group of halogen-containing compounds (HCC): chloroform, dichlorobromo-methane, dibromochloro-methane, tetrachloroethylene and others, very frequently found in drinking water. The presence of these compounds in drinking water is caused either by their formation in the course of water chlorination at the waterworks treatment plants or by the pollution of water bodies with sewage water containing these substances as a result of chlorination for the purpose of sewage water decontamination, or as a result of industrial use and production of HCC.

The problem of HCC formation, in particular the formation of trihalomethanes (THM) in the course of water chlorination first attracted public notice in 1974 following the appearance of papers by Rook and Bellar who demonstrated that chlorinated drinking water contains a considerable proportion of chloroform and other THM.

Although low-molecular organochlorine substances had been previously detected in natural water (e.g., carbon tetrachloride and dichloroethane), Rook was the first to relate the content of THM in drinking water to the process of its chlorination. He detected THM in the chlorinated water of the Rhine used for Rotterdam's water supply. The water contains a large quantity of fulvic acids and humin bases and is chlorinated beyond the inflection point. According to his research, the content of chloroform reached 100 µg/kg, and that of other HCO ranged from 5 to 25 µg/l.

In the same year Bellar with co-workers developed a technique making it possible to quantify the amounts of volatile HCO to within a few nanograms. They confirmed the presence of THM in chlorinated tap water. The highest THM content (37-150 µg/l) was found in drinking water pumped from surface water bodies. These compounds found their way into the water as a result of its chlorination, and the main factor responsible for their formation was the presence of free chlorine in the water.

In this connection serious concern for the health of the people was aroused by the report of Harris and Page (quot. from Marx, 1974) who found cancer morbidity and mortality among the population of the US state of Louisiana using chlorinated water of the Mississippi as the source of their water supply to be 15% higher than cancer mortality of people living in the same state but using ground water. In consequence, a suspicion was voiced that possible organic pollution of the Mississippi river may serve as the etiological factor responsible for the higher cancer morbidity among Louisiana's population. This assumption was confirmed after the finding of 66 organic compounds including HCC in the drinking water of New Orleans such as carbon tetrachloride, chloroform, chloroethane, dichloroethane, etc., with the chloroform concentrations reaching 100 μg/l. In vivo experiments showed this chloroform to be quite an active carcinogene: prolonged chloroform exposure to doses of 50 and 100 mg/kg produced frequent (up to 57 per cent) formation of hepatocellular carcinomas in mice, and of thyroid cancer and renal epithelial tumors in rats (Page, Saffioti, 1976; Cantor, Mc.Cabe, 1978; Csanadi, 1978).

A characteristic feature of this study, which hightened well the interest in the water chlorination problem, was the discovery of the fact that the HCC content in the chlorinated drinking water of New Orleans water-supply was several times as high as that in the untreated water of the Mississippi.

The report of Harris and Page was the first in the subsequent series of epidemiological observations aimed at ascertaining the correlations between malignant neoplastic morbidity and water chlorination. The results of these studies are presented in the papers by De Rouen, Diem (1977), Buncher et al. (1977), Cantor et al. (1977, 1978), Muller (1978), and other authors who analyzed possible correlations between cancer mortality among the people of 932 districts in the USA and drinking water chlorination, with due attention to the impact of socio-economic and demographic factors as well as the extent of industrialization over the period of 1950-1977. As a result, positive correlations were ascertained for the tumors of the urinary bladder, the brain, kidneys and rectum. In the opinion of Buncher et al. (1977), drinking water chlorination in the Ohio river basin is the cause of at least 50 lethal cases of cancer per year.

To exclude the possible impact on cancer mortality of carcinogenic compounds unconnected with the water chlorination process, all water-supply sources were investigated to find out whether they contained possible corcinogenes: arsenic, cadmium, lead, nickel, etc. In no case did the amounts of these substances in water exceed their maximum permissible concentrations (MPC), nor were any correlations established between their concentration and cancer mortality. This study is by itself of no small importance in terms of checking the reliability of the hygienic ratings recommended for the chemical substances recently suspected of acting as potential carcinogenes. These data, although produced by a single study, indicate that the content of the above substances in drinking water at the level of, or below their MPC can obviously be regarded as oncologically safe, in other words, the maintenance of hygienic MPC for suspect carcinogenes is one of the major factors preventing the possibility of tumor formation provoked by these substances.

Analysis of the above oncoepidemiological studies reveals a great similarity in the results of the investigations performed by different authors, and also suggests that the mortality levels due to the cancer of the urinary bladder and the gastroenteric tract presently observed in the USA is directly associated with drinking-water chlorination. Investigations performed by Muller (1978) led the author to the conclusion that water chlorination in Germany causes a certain increase in the incidence of gastroenteric cancer. These observations increase the probability of the assumptions that there actually exists an interdependence between water chlorination and the risk of cancer morbidity among the people exposed to this water for a long time.

Indeed, the results of numerous recent investigations indicate that in consequence of the interaction between chlorine and the organic substances polluting the water of natural and technogenic origin, a considerable number of HCC are formed; the carcinogenic activity of some of them has been already established and that of the others is still being studied.

In samples of drinking water obtained by means of surface water chlorination the maximum detected THM concentration amounts to 850 μg/l, and that of chloroform - 815 μg/l.

It is practically impossible to determine the average concentration of these substances in water from the data published by different authors; one can, however, say that most of the tested drinking-water samples have THM concentrations of the order of 100-300 μg/l. Besides chloroform other substances were: bromodichloromethane (maximum concentration 270 μg/l), dibromochloromethane (184 μg/l), bromoform (92 μg/l). In chlorinated artesian water samples the content of THM is markedly lower - up to 12 μg/l. Along with highly volatile HCC having only 1-2 carbon atoms to the molecule, chlorine aromatic compounds and pesticides have also been found in the drinking water.

The maximum levels of HCC content in water are by more than

2 orders of magnitude lower than the MPC for certain substances, established, as a rule, on the basis of the organoleptic indications of harmfulness. Therefore, the problem of studying the general toxic properties of HCC is not a task of primary importance. At the same time, the absence of odour in drinking water, which indicates that the content of these substances in it is below MPC, does not completely guarantee its safe use. This, as was already noted, is proved by epidemiological observations revealing an increase in the oncological morbidity when chlorinated water containing halogen-substituted hydrocarbons is used. From this follows the necessity of revising the existing MPC of HCC and elaborating MPC for other substances in this series, with an emphasis placed on studying blastomogenic and mutagenic activity.

It has been established in a number of studies, some HCC, in particular, trichloroethylene, dibromochloropropane, tetrachlorophenol hydroxide, polychlorinated biphenyls, manifest embryotoxic effect, including teratogenic properties (Dorfmueller et al., 1979; Rudic, Newsome, 1979; Reggiani, 1978; Yamashito, 1977). Far from enough work, however, has been carried out in this direction for one to arrive at any general conclusions and extend them to cover the whole HCC group. Nevertheless, these findings have to be taken into account in elaborating the hygienic ratings for the above substances in the water of reservoirs.

Research results show different content levels for the same halogen-substituted substances found in chlorinated water. This is due to different causes, some of which have been ascertained, while others require verification. In particular, in water chlorination the intensity of trihalomethane formations from natural water humic compounds is determined by the concentration of these organic substances and their qualitative composition, pH and t° of the medium, the nature (form) of the desinfecting agent, Cl_2-C ratio, etc. (Cristman et al., 1978; Morris, Baum, 1978).

A broad spectrum of HCC found in drinking water and an increase in the incidence of carncer, caused by its consumption, raise the question of whether it is chlorination that actually leads to the appearance of carcinogenically active substances in the water. One can give a positive answer to this question only after proving the carcinogenic and mutagenic properties of these substances in in vivo experiments. Investigators in many countries are looking for answers to these questions.

Chloroform, whose carcinogenic properties have already been mentioned, and dichloroethane are among the best studied in this respect. Scores of papers have been devoted to studying the carcinogenic and mutagenic activity of dichloroethane (Rannung, Remel, 1977; Maltoni, 1977; Viola, Caputo, 1977; Bahlman et al., 1979; Parker et al. 1979; Laib et al., 1979 and others). As a result of these studies, despite some failures in inducing tumors in experimental animals, it was established that, when administered inhalatorily and intragastrically, dichloroethane in doses from 25 to mg/kg induced tumors of the pregastrum, lungs, spleen, mammary gland and uterus in 6-36% of the experimental rats and mice. The tumors were represented by highly malignant hepato- and adenosarcomas, adenocarcinomas and planocellular forms.

Blastomogenic activity has been ascertained in hexachlorobenzene entering the organism of Swiss mice with feed (Cabral et al., 1979), trichloroethane, tetrachloroethane and hexachloroethane (Parker et al., 1979), tetrachlorophenol hydroxide (Reggiani, 1978) and other HCC. Of no small importance is the fact that a number of studies have established a direct carcinogenic effect of some HCC (chlordene, penta- and heptachlor) on the human organism (Infante et al., 1978). In spite of this, fact the data available today are as yet insufficient for the final conclusion on the extent of carcinogenic hazard of HCC present in drinking water.

Since the classical techniques of ascertaining the carcinogenic activity of chemical substances in vivo experiments are labor consuming and, more importantly time-consuming, while, at same time, the interrelation between the carcinogenic and the mutagenic effects can be regarded as a firmly established fact (the data of different authors show that out of all investigated carcinogenic substances more than 90% manifest clearly expressed mutagenic properties (Deseres, 1978), many of HCC have been tested for their mutagenicity with the help of fast bacterial tests. For instance, Gogelman and co-workers, who studied in 1978 the mutagenic effect of tetrapenta- and hexachlorodienes on E.Coli-12 in the presence or absence of microsomal activating system, established a high frequency of direct mutations of resistance to 5-methyltriptophane and back mutations from arginine auxotrophity to prototrophity. In the Ames tests mutagenic activity was revealed for numerous representatives of chloroethanes, chloroethylenes, chlorobutadienes and other HCC (Bartch et al., 1979; Rannung, Remel, 1977; Infante, 1977; Simmon and Tardiff, 1978). These authors examined the mutagenic activity of a number of halogen-substituted hydrocarbons fond in chlorinated drinking water, using the Ames test with or without microsomal fraction. It turned out that 7 out of the 9 known carcinogenes had mutagenic activity (vinyl chloride, vinilidene chloride, trichloroethylene, 1,2-dichloroethane, bromoform, methyl iodide and bis (2-chloroethyl) ether), as well as a number of compounds whose carcinogenic activity was not studied or not ascertained (bromodichloromethane, dibromochloromethane, methylene chloride, bromochloromethane, 2-chloropropane and others).

Since the identification of HCC present in water appears to be an extremely complicated task the question arises of how to assess the degree of carcinogenic hazard posed by the whole range of chemical substances formed in water chlorination and isolated from water through concentration. Such investigations have a number of advantages because they make it possible to estimate the combined effect, the carcinogenic and the co-carcinogenic action of substances at the same time.

In this connection, the work of Loper with co-authors (1978) is of considerable interest. From drinking-water samples of 5 large US cities extracts of residual organic matter were obtained, which were tested for mutagenicity in the Ames test and by the tissue culture method. Mutagenic activity was found in all the extracts obtained from all the samples of 5 water-supply systems, with the spontaneous level of mutagenesis on different Salmonella cultures exceeded 10-fold or less. One sample out of 5 transformed the VALB/3T3 cell culture, producing cells with a propensity for tumoral growth. The results were identical even if water samples from the same water-supply system were taken within the interval of 2-3 months. The results of this investigation open up new aspects in estimating health hazard for the population from organic pollutants of drinking water, including HCC.

Apart from direct biological effects (mutagenic, carcinogenic, embryotoxic) associated with water chlorination, there exists a real danger of public health being indirectly affected by chlorination, e.g., because of the appearance of chlorine-resistant bacterial and viral forms (Bates et al., 1977; Hoehn et al., 1977 and others).

Different authors have discussed the two most probable mechanisms of the appearance of chlorine-resistant forms: I - selection of a resistant subpopulation among the parental clones and 2 - direct mutagenic effect of chlorine on the induction of resistant variants. The greatest significance of these works seems to lie in the fact that, in the course of adaptation to chlorine, changes are taking place in such phenotypic characteristics as the size and shape of plaques, the morphology and virulence of viruses. These changes can have serious consequences for the health of the people if large groups are exposed to such resistant forms found in drinking water ready for consumption (McDermott, 1975; Van der Velde, 1973). Appearance of chlorine-resistant forms among the pathogenic bacteria of the intestinal group can reduce the significance of E.Coli as a health indicator and create a threat of aquatic epidemic outbreaks of infectious diseases of non-viral etiology.

Moreover, there exist convincing data indicating that HCC formed during chlorination may constitute a health hazard for the population via their inclusion in the trophodynamic chain, e.g., algae (plankton) - crustaceans - fishes - man (Erb et al. 1978; Ericson, 1980 and others). The content of HCC, in particular, of certain pesticides, polychlorinated biphenyls, in the flesh and liver of fish go up as high as several milligrammes/kg of the weight of fish, depending on the value of octanol/water partition coefficient (Chiou et al., 1977, Olson et al., 1978). That such a possibility exists has been convincingly proved by a "pool" of a number of organochlorine compounds, with polychlorinated biphenyls among them, discovered in the subcutaneous fat of the inhabitants of Greenland and Denmark and the establishment of a correlation between their amounts in the fatty tissue and their levels in the fish eaten by the people. Also of interest is the fact that the content of chlorinated hydrocarbons in fish, algae and plankton is closely correlated with their content in benthic deposits.

Among possible consequences of water chlorination are the unfavourable effects of active chlorine and a number of chlorine-substituted hydrocarbons upon aquatic flora and fauna (Dickson et al., 1977; Toets et al., 1977; Cherry et al.1977; Ericson and Freeman, 1978; Brooks and Seegert, 1978, and others). The impact of chlorine on higher aquatic organisms (fishes) has manifested itself in different biological effects;

branchial hyperplasis and the swelling of lamellar epithelial cells, deterioration of cardiac activity and hyperventillation, formation of complex behavioral reactions, changes of habitat areas, loss of ability to gather into shoals (Heath, 1977, 1978; Greev et al., 1978; Larric et al., 1978; Bogardus and Boies, 1978).

The data presented above are quite sufficient to regard the problem of drinking-water chlorination as an independent, important and complex one within the general task of producing safe water.

Having summed up the above account one can arrive at the conclusion that the general objective in solving the water chlorination problem is the exclusion of unfavourable effects on the health of the population, i.e. the possibility of cancerous and other chronic diseases being caused by the consumption of drinking water containing HCC.

The attainment of this objective is possible, provided a number of problems are solved:

1. To further study the mechanism of HCC formation in drinking water when it is decontaminated with chlorine, which makes it necessary to elaborate highly sensitive physico-chemical methods for the identification of the compounds formed.

2. To investigate in depth drinking-water quality in water-supply systems, in order to identify the range of products formed in the course of chlorination and their actual concentrations in water, depending on the amount of humic and organic compounds.

3. To arrange and order the information on the biological

activity of chlorinated products, including the data on their toxicity, carcinogenic and mutagenic activity, stability in water, capability of affecting the organoleptic properties of water and the aquatic ecological systems.

4. To draw up a priority list of organochlorine compounds for subsequent toxicologic-hygienic microbiological and ecological study with the aim of establishing their maximum permissible concentrations.

In conclusion it should be emphasized that the representatives of public health bodies together with engineers and technicians will have to a solve a host of problems associated with water supply on a case-by-case basis and relative to the local situation. Irrespective of the outcome of the above studies, in the final analysis citizens must receive high-grade water meeting the drinking water standard. If such a standard is not available recommendations for the quality of drinking water should be enforced.

REFERENCES

1. Bahlman L., Leidel N., Parker J. Amer. Ind. Hyg. Ass. J., 1979, 2, 395.
2. Bartsch H., Malaveille C., Barbin A., Archiv Toxicol., 1979, 39, 9, A-35, A-37, A-39.
3. Bates R., Shaffter T., Sutherland S. Appl. Environm. Microbiol., 1977, 34, 849.
4. Bellar T., Lichtenberg I., Kroner R. J. Amer. Water Works Ass., 1974, 66, 12, 703.
5. Bogardus R., Boies D. Water Chlorination, Environmental Impact and Health Effects, 1978, 2, 95.
6. Brooks A., Seegert G. Ibid., 115.
7. Buncher C., Kuzuma R., Forcade C. Origins of Hum. Cancer. Book A. Incidence Cancer Hum. Cold Spring Harbor, 1977,p.347
8. Cabral J., Muller T., Raitano F., Shubic P. Intern. J. Cancer, 1979, 23, I, 45.
9. Cantor K., Hoover R., Mason T., Ma Cabe L. Amer. J. Epidemiol., 1977, 106, 230.
10. Cantor K., McCabe L. Water Chlorination, Environmental Impact and Health Effects, 1978, 2, 379.
11. Cherri D., Larric S., Dicson K., Hochn R., Cairns J.J.Fish. Res., Bd. Canada, 1977, 34, 1365.
12. Chiou C., Freed V., Schmeddling D., Kohnert R. Environm. Sci. Technol., 1977, 11, 475.
13. Christman R., Johnson, Hass, Pfender F., Alexander H. Water Chlorination, Environmental Impact and Health Effects, 1978, 2, 15.

14. Cszanadi M. Egeszsegtudomany, 1978, 22, 2, 146.

15. De Rouen T., Diem J. Origins of Hum. Cancer. Book A. Incidence Cancer Hum. Cold Springs Harbor, 1977, p.331.

16. Dicson K., Cairns J., Gregg B.J., Water Poll. Control Fed., 1977, 49, 34.

17. Dorfmueller M., Henne S., York R., Bornschneir R., Manson J. Toxicology, 1979, 14, 2, 153.

18. Erb F., Doquidt J., Cazin J., Brice A., David D., Colein P.Techn. Sci. Municip., 1978, 73, 3, 117.

19. Ericson S., Freeman A. Water Chlorination. Environmental Impact and Health Effects, 1978, 2, p.307.

20. Gogleman W., Bonse G., Henschler D., Creim H. Biochem. Pharmacol., 1978, 27, 24, 2927.

21. Greeve J., Johnston L., Dunstall T., Minor J. Water Chlorination, Environmental Impact and Health Effects, 1978, 2, p.77.

22. Heath A.G. Hydrobiologia, 1977, 56, 39.

23. Heath A.G. Water Chlorination, Environmental Impact and Health Effects, 1978, 2, p.123.

24. Heath C.W. Environm. Health Perspect., 1978, 27, 7.

25. Higginson J., Callum S. Cancer Detection and Prevention, 1976, I, I, 79.

26. Hoehn R., Randal C., Bell F., Shafter T.J. Environm. Eng. Div., 1977, 103, 803.

27. Infante P.N. Environm. Health Perspect., 1977, 21, 251.

28. Infante P.N., Epstein S., Newton W. Scand. J. Work Environm. Hlth, 1978, 4,2, 137.

29. Korolev A.A. Gigiyena i sanitariya, 1976, 3,103(in Russian)

30. Laib R., Stockle G., Bolt H., Kunz W.J. Cancer Res. Clin. Oncol., 1979, 94, 2, 139.

31. Larrick S., Cherry D., Dickson K., Cairns J.Water Chlorination, Environmental Impact and Health Effects,1978,2,135.

32. Loper J., Lang D., Smith C. Ibid., p.433.

33. Maltoni C. Environm. Health Perspect., 1977, 21, 5.

34. Marx P. Science, 1974, 186, 809.

35. McDermott J.H. J. Amer. Water Works Ass.,1974,66,693.

36. Mikhailovsky N.Ya. Ilnitsky A.P., Korolev A.A. Kazanskiy med. zhurnal, 1979, 6, 65 (in Russian).

37. Morris J.C. Water Chlorination, Environmental Impact and Health Effects, 1978, 2, p.879.

38. Müller G. Ibid., p. 483.

39. Olson M., Jensen S., Reutengard L. AMBIO, 1978, 2, 66.

40. Page N.P., Saffioti U. Report on Carcinogenesis Bioassay of Chloroform. Bethesda, Maryland: National Cancer Institute, 1976.

41. Parker J., Casey G., Bahlman L., Leidel N., Rose D.,Stein H., Lane J. Amer. Industr. Hyg. Ass. J., 1979,40,3,A-46,A-57

42. Rannung U., Sundvall A., Ramel C.J. Toxicol. Environm.Hlth., 1977, 2,5, 1019.

43. Reggiani G. Archiv Toxicol., 1978, 40,3, 161.

44. Ruddic K., Newsome W. Bull. Environm., Contamin. Toxicol., 1979, 21, 4-5, p.509.

45. Simon W., Tardiff R. Water Chlorination, Environmental Impact and Health Effects. 1978, 2, p.417.

46. Toetz D., Varga L., Pierce M. Water Res., 1979, II,3,253.

47. Van der Velde T.L.J.Amer. Water Works Ass.,1973,65,345.

48. Viola P.L., Caputo A. Environm. Health Perspect.,1977,21.

49. Yamashito F. Paediatrician, 1977, 6, 1, p.20.

TOXICITY ASSESSMENT OF NITROGEN-CONTAINING SUBSTANCES IN TERMS OF WATER HYGIENE STANDARDS (IN RELATION TO APPLICATION OF FERTILIZERS)

L.Y. Vasyukovitch

Identifying and abating the harmful effects of nitrogen-containing substances on human health is a necessary element of environmental sanitation. Such substances as nitrates, constituting a regular component of potable water, are introduced into it primarily by way of water runoff from cultivated and fertilized lands, as well as by communal sewage.

In real life, both nitrates and nitrites are normally found in water. Their relation in water bodies depends upon the activity of nitrite- and nitrate-forming bacteria.

A substantiation of preventive measures ensuring the sanitary protection of water bodies requires the establishment of hygienic ratings for acceptable levels of nitrogen-containing compounds in water. Since nitrates are usually accompanied by nitrites, it is appropriate to include a hygienic rating for the total content of these nitrogen-containing substances into the standard of water quality.

The fact that these substances are not equivalent in toxicity levels, while having much in common in terms of their toxic effect mechanisms, means that their comparative toxicity coefficient should be found. Several approaches were used to this end.

1. By using the relation between DL_{50} values. This factor varies over a wide range, from 10 to 30 times for test animals and from 6 to 44 times for man, this being, apparently, accounted for by differences in age, sex and conditions of test animal

keeping (19; 21).

2. By collating allowable daily doses. According to FAO-WHO data, a daily nitrate dose in man's food diet should not exceed 0.5 mg and that of nitrate - 5 mg, i.e. the factor of difference in their toxicity is equal to 10.

3. By comparing maximum allowable concentrations of nitrites and nitrates. Nitrates are rated at a level of 10 mg/l (7). There is no nitrite rating for drinking water in the USSR National Standard. The toxicity of nitrates is known to depend on nitrites, which are directly responsible for the pathogenesis of methemoglobinemia and adverse health effects. Hence the need for studies to be conducted to establish a maximum allowable nitrite concentration in water which permitted us to recommend a suitable concentration at a level of 1 mg/l by the toxicological criterion of harmfulness (1; 5). In establishing the maximum allowable concentration it was found that, apart from the systemic effect,nitrite also has a gonadotoxic effect occurring at higher levels of exposure with concentrations of 5 mg/l, decreasing the spermatozoon count down to one third.

In our studies (9) an attempt was made (in establishing such optimal conditions for tumour formation as the use of non-vitaminized food and of a very sensitive animal species - white rats, optimum relation between secondary amine (5 mg per litre of proline) and nitrite (0.05 mg per kg of animal weight in terms of nitrogen) - to test the tumour inducing capability of nitrate, rated at the recommended level of 1 mg/l, over a two-year experimentation period. According to theoretical calculations, a daily dose of 0.05 mg/kg of nitrite may, under optimum conditions, form 1.2 γ of nitrosamine (17), and, according to Drukerey's data (18), a minimum dose of nitrosamine, capable of generating a tumour at the end of the life-span in rats, is 75 γ /kg, i.e. 75 times higher.

Considering that the effect of the carcinogenic dose does not practically differ with the species, it may be assumed that threshold doses, inducing tumours in various species of mammals, including man, are also close to each other. Hence, the recommended hygienic standard for nitrite rated at a level of 1 mg/l, may be safe in terms of the carcinogenic effect. Naturally, for safe levels of nitrite to be specified, data need to be accumulated from epidemiological studies on oncological diseases among those consuming nitrite- or nitrate-polluted water (20).

Thus, according to the relation between the maximum allowable cocentration of nitrites, established at a level of 1 mg/l (5), and that of nitrates (10 mg/l (7)), their toxicity differs by a factor of 10, thus permitting us to suggest the following formula for rating the total level of nitrites and nitrates in water:

$$C_1 + 0.1\, C_2 = 1 \text{ or } 10\, C_1 + C_2 = 10 \quad (1),$$

where C_1 is nitrite concentration; C_2 is nitrate concentration in mg/l (5).

A possible simultaneous exposure to nitrogen-containing substances from different media necessitates the establishment of hygiene-based principles and methods for rating a maximum permissible load (MPL) as an integral criterion of environmental quality (15).

The maximum permissible load was determined by establishing the relative biological activity of substances, introduced into the organism from different media (6) and taking account of the fact that the toxicity of even one substance, introduced into the organism with water and in a bound form with food, may be varied (13).

At the first stage of establishing the maximum permissible load of nitrites and nitrates, contained in water and food ingested by man, the maximum allowable daily dose of nitrate for adults was rated at a level of 200 mg NO_3 per day (or 45 mg in terms of nitrogen), i.e. 4 mg/kg of nitrate in terms of NO_3, assuming man's weight to be 50 kg (12). The scientific validity of this dose, as well as its possible treatment as a maximum non-effective (subthreshold) dose, is confirmed by WHO's recommendations (WHO series of technical reports No. 228, 1963, p. 85) where the value up to 5 mg/kg in terms of NO_3 is given as an absolutely allowable man's daily dose. Taking into account the calculated coefficients of comparative biological activity (K_2 equal to 0.8 and K_3 equal to 40, characterizing the comparative toxicity of nitrate, ingested with food and water, and nitrites and nitrates in food, respectively (13)), a general formula was deduced to calculate the maximum allowable daily dose (MADD) (10):

$$\text{MADD} = \frac{T_{1DR} + K_3 T_{2DR}}{F_2} + 3\,(T_{1W} + F_1 \cdot T_{2W}) \qquad (2)$$

where MADD = 45 mg in terms of nitrate nitrogen;

T_{1DR} and T_{2DR} are total nitrate and nitrite concentrations (in mg) in man's daily food ration in terms of nitrogen;

T_{1W} and T_{2W} are respective concentrations of nitrate and nitrite (in mg/l) in water;

3 is an adult's daily water consumption (1);

F_1, F_2, F_3 are factors of comparative biological activity.

Substituting the value of factors, we derive:

$$45 = \frac{T_{1DR} + 40\ T_{2DR}}{0.8} + 3\ (T_{1W} + 10\ T_{2W}) \qquad (3)$$

Upon the simplest mathematical transformation the equation takes the following form:

$$T_{1DR} + 40\ T_{2DR} + 2.4\ (T_{1W} + 10\ T_{2W}) = 36 \qquad (4)$$

The suggested equation (3) provides the basis for a simple calculation of allowable amounts of nitrogen-containing substances, to be ingested with food, thus permitting the organized population contingents to make up a nitrite- and nitrate-safe diet by varying composition and volume of constituent foodstuffs for consumption. At the same time it opens up a possibility of establishing permissible residual equantities on a regional basis (13).

In calculating the maximum permissible load of nitrites and nitrates for children under scholl age, the value of maximum allowable daily dose may be determined from the child's weight and a relatively higher consumption by children of both water (twice as much) and food (twice as much) compared to that of adults per one kilogram of weight (11). Consequently, in computations of the maximum allowable daily dose, it is expedient to make use of the value equalling 0.225 mg/kg (45 mg : 50 mg : 4 = 0.225 mg/kg) by introducing a correction factor = 4 into the equation.

It should be noted that equation (3) is applicable for the determination of safe concentrations of nitrites and nitrates with respect to the adult population living in temperate climatic and geographical zones. In southern regions, the water consumption factor is increased by 1.25 times (zone III) and 2.1

times (zone IV), considering a variable pattern of water consumption in different climatic and geographical regions, i.e. for zones III and IV, instead of the daily water consumption factor equalling 3 it is appropriate to apply the factors 3.75 and 6.3 respectively.

In real life, whatever the environmental medium (water, foodstuffs, air) of transference of toxic substances, exposure patterns may quite often assume an intermittent character. This is accounted for by water and food being taken at intervals and polluted to a variable degree. Specific modes of water consumption and specific conditions of work are additional factors, contributing to varied effects of chemicals on health.

The lack, in water hygiene, of clear-cut quantitative methods for assessing these exposures prompted us (8) to develop criteria and methods of assessing the intermittent effect of substances through the application of isoeffective dose-rates of the $ED_N \pm M$ type, calculated by using the probit-analysis method on the basis of the dose-effect relation. High-cumulative (sulfidophos) and low-cumulative (nitrate) chemicals were used as model substances through their intermittent and continuous peroral introduction in permanent and variable concentrations to white rats. To ensure comparability of experimental results, provision was made for maintaining the equality of doses, accumulated over similar periods of exposure (a weeklong cycle) under variable conditions of ingestion of the chemical compounds under study.

These investigations (8) permitted us to suggest the following criteria for comparing different modes of exposure to chemical substances: 1) the study of intoxication dynamics with re-

gard to the chosen temporal cycles and the assessment of the relationship between the toxic and compensatory processes;
2) the application of isoeffective values of the $ED_N \pm M$ type, computed after a regular cycle of exposure, for quantitative comparison of intoxication severity in the case of different modes of exposure to chemical substances.

It is noteworthy that research-based ratings for appropriate levels of nitrogen-containing compounds in water are usually established on the basis of the healthy organism model, disregarding the pathogenetic factors of diseases - the role of intestinal nitrate-reducing microflora, i.e. collibacilli, purulent staphylococci and other microorganisms.

An increase in the toxic effect of nitrates through their more intensive reduction by the gastroenteric tract's microflora was observed by us (2) in modelling dyspepsia in test animals.

The increased toxicity of nitrates, in cases of their being ingested in combination with E.coli (2), may hygienically be treated as a risk factor, capable of aggravating the pathogenesis of intoxication. Consequently, the acceptable levels of nitrates in water should be primarily determined for groups of persons with dispeptic disturbances.

In recent years, the hygienic rating of nitrogen-containing substances has become even more complicated because of their possible impact in combination with pesticides which are being used in ever increasing amounts due to the intensive chemicalization of agriculture.

Our experiments (4) included the comparative studies on assessing the combined toxic effect of fertilizers and pesticides using the nitrite and sulfidofos model, as against their individual effects, by collating the values of isoeffective doses of the $ED_N \pm M$ type, calculated by the probit-analysis method on the basis of the dose-effect relation and registering the count of methemoglobine and cholin esterase activity in the animals' blood.

The development of quantitative criteria to assess the combined effect of fertilizers and pesticides permitted us to recommend that toxicological studies be conducted on the basis of the principle of isoequivalence of their biological activity. In this case a quantitative assessment has to be made with due regard for the results of studying the substance's toxic effect, analyzed not by a single temporal point but by registering the phases of the toxicodynamic process evolution.

Hygienic requirements stipulate an allowable concentration of a chemical substance in water bodies as being not only safe in terms of health effects, but also as leaving the organoleptic properties of water intact and having no effect on the sanitary conditions of water bodies. Impairment of sanitary conditions also impedes the process of natural self-cleaning of water in reservoirs, thus leading to constraints in terms of household and recreational water uses. That is why provision is made for studying effects of harmful substances on the BOD and nitrification process. However, the negative consequences of water reservoir eutrophication caused by nitrogen-containing biogenous substances, should also be considered. Eutrophication is responsible for the deterioration of the organoleptic properties of water, the accumulation of toxic products (such as cyanides) and other factors which have aquired alarming proportions in several water reservoirs throughout the world and generated in adverse impact in terms of water supply and household and recreational water uses. Consequently, reducing the level of biogenous nitrogen-containing substances in water would also be beneficial from the hygienic standpoint.

According to US studies, the ecological rating for inorganic nitrogen is fixed at a level of 0.3-0.5 mg/l (24). With reference to this country, these values have probably to be treated as tentative and requiring correction considering the nitrogen/phosphorus relation for water and the regional features of water reservoirs. Thus, depending on the use of a water reservoir (type of water use), the following ratings may be taken for reference (Table 1).

Table 1. Ratings for nitrogen-containing substances

Nitrogen-containing substances	Ratings (mg/l)		
	hygienic	fishery	ecological
Nitrogen of nitrites	1	0.02	0.3-0.5
Nitrogen of nitrates	10	9.1	
Ammonia	2	0.05	

When a water reservoir caters for several users, a lesser value should be taken for reference (3). In doing so, it would be possible to ensure the preservation and rational use of water in reservoirs. The practical application of such a scale of ratings will permit us to formulate more stringent requirements with regard to the disposal into water reservoirs of both industrial effluents and rain water flooding croplands.

These data make it clear that hygienic problems caused by the application of nitrogen-containing fertilizers, require a comprehensive study. It is primarily necessary for safe hygiene standards to be recommended ensuring a healthy environment in the interests of the present and future generations, as well as for the development of scientifically substantiated periods and rates of application of mineral fertilizers which are major sources of water pollutants by nitrogen-containing substances.

REFERENCE

1. L.Y. Vasyukovitch; M.A. Bobyleva. In collection "Sovremennye voprosy gigieny vodnogo transporta" (Contemporary Problems of Water Transport Hygiene), Moscow, 1975, pp. 298-299.
2. L.Y. Vasyukovitch; A.N. Zakharkina. In collection "Voprosy okhrany okruzhayushei sredy" (Problems of Environmental Protection), Perm, 1977, pp. 56-57.
3. L.Y. Vasyukovitch; G.N. Krasovsky. In collection "Antropogennoye evtrofirovanie prirodnykh vod" (Cultural Eutrophication of Natural Waters), Chernogolovka, 1977, p. II, pp.283-285.
4. L.Y. Vasyukovitch; G.N. Krasovsky. In collection "Gigienicheskie i biologicheskie aspecty primenenia pestitsdiov v usloviyakh Srednei Asii i Kazakhstana" (Hygienic and Biological Aspects of Pesticide Use in Central Asia and Kazakhstan), Dushanbe, 1978, pp. 14-15.
5. L.Y. Vasyukovitch; G.N. Krasovsky. "Gigiena i sanitaria" (Hygiene and Sanitation), 1979, No. 7, pp. 8-11
6. L.Y. Vasyukovitch; G.N. Krasovsky; H.I. Lutsoya; V.T. Mitchenkov; M.Y. Rooma; B.V. Karochkin. In collection "Mineralnie udobrenia i kachestvo pischevykh productov" (Mineral Fer-

tilizers and Quality of Foodstuffs), Tallin, 1980, pp. 28-29.

7. Sh.H. Kapanadze. Materialy k gigienicheskomu obosnovaniyu PDK nitrate v vode (Materials for Hygienically-based Maximum Allowable Concentration of Nitrate in Water), Ph.D. (medicine) dissertation. Tbilisi, 1964.
8. G.N. Krasovsky; L.Y. Vasyukovitch. In collection "Gigienicheskie aspekty okhrany okruzhayuschei sredy" (Hygienic Aspects of Environmental Protection), Moscow, 1978, No. 6, pp. 60-61.
9. G.N. Krasovsky; L.Y. Vasyukovitch. In collection "Kantserogennie nitrosoedinenia-deistvie, obrazovanie, opredelenie" (Carcinogenic Nitrocompounds—Their Effect, Formation and Definition), Tallinn, 1978, pp. 175-176.
10. G.N. Krasovsky; L.Y. Vasyukovitch; H.I. Lutsoya; V.T. Mitchenkov; M.Y. Rooma. "Gigiena i sanitariya" (Hygiene and Sanitation), 1982, No. 4, pp. 23-24.
11. G.N. Krasovsky; E.E. Sarkisyants; A.Z. Belousov; N.A. Egorova. Materialy vsesouznogo simpoziuma po izucheniyu vliyaniya khimicheskikh veschestv na molodoi organizm i voprosam vozrastnoi teksikologii (Materials of the National Symposium on a Study of Young Organism's Exposure to Chemical Substances and Problems of Age-Related Toxicology), Moscow, 1969, pp. 119-126.
12. V.T. Mitchenkov. Sbornik tezisov dokladov III respublikanskogo syezda epidemiologov, microbiologov, infektsionistov i gigienistov ESSR (Collection of Theses of Reports Submitted to the III Estonian Republic's Congress of Epidemiologists, Microbiologists, Hygienists and Infection Specialists of the

Estonian Soviet Republic), Tallinn, 1977, pp. 339-340.

13. V.T. Mitchenkov. Sbornik tezisov dokladov respublikanskogo simpoziuma "Mineralnye udobreniya i kachestvo pischevykh produktov" (Collection of Theses of Reports Submitted to the Republic's Symposium on Mineral Fertilizers and Quality of Foodstuffs), Tallinn, 1980, pp. 100-106.

14. WHO series of technical reports. 1962, No. 228, pp. 83-87.

15. G.I. Sidorenko. "Gigiena i sanitariya" (Hygiene and Sanitation), 1978, No. 10, pp. 9-15.

16. N.A. Yavorsky. In collection "Vsestoronniyi analiz okruzhauschei sredy" (A Comprehensive Environmental Analysis), Leningrad, 1975, pp. 189-206.

17. K. Simon; Z. Knotek; J. Shmid Musya. "Gigiena i sanitaria" (Hygiene and Sanitation), 1963, No. 10, pp. 7-13.

18. V. Mukha; P. Kamensky; K. Keleti. "Gigiena i sanitaria" (Hygiene and Sanitation), 1965, No. 8, pp. 16-20.

19. M.N. Tarasov; A.S. Demchenko; L.V. Brazhnikova. Report to the USSR Symposium on Cultural Eutrophication of Water Bodies, Chernogolovka, 1974, pp. 39-44.

20. D. Ulman; T. Brighting. "Memorandum of the Symposium on the Effect of Fertilizers in Terms of Water Quality", Berlin, 1973, pp. 3-14.

21. Ridder W.E.; Oehme F.N.-Clin. Toxicology, 1974, pp. 7, 145-149.

PECULIARITIES OF TOXICOLOGICAL ASSESSMENT OF AIR POLLUTANTS

M.A.Pinigin

INTRODUCTION

The atmospheric air hygiene as a scientific discipline is relatively young compared with other hygienic sciences. However, in recent years, it has gained much prominence due to the increasingly acute problem of atmospheric air pollution control. The emphasis laid on the hygienic regulation of the allowable content of air pollutants, as a scientific basis for remedial and preventive measures, is of primary importance for the development of the atmospheric air hygiene.

At present, the MACs cover 256 chemical compounds and the combined effect of 43 mixtures, consisting of 2, 3 or 4 substances.

The hygienic regulation of the MACs in the air environment is based on the experimental study of their biological effect, i.e. the toxicological assessment which is quite distinct from the assessment of pollutants in water bodies, industrial premises, etc.

The peculiar features of the principles, criteria and methods of assessing noxious substances in the atmosphere of communities are determined primarily by the atmospheric pollutants' impact on the environment and the people's comfort, and the possibility of its round-the-clock and long-term impact on the population, including its most vulnerable groups (children, the aged and the weak).

The regulation of the allowable content of chemical agents is based on the concept of thresholds in their action though the thresholds (concentrations) themselves are relative and are determined by many factors both physical (the aggregate condition of the substance, the environment, the regime, the duration of exposure, etc.) and biological (the physiological condition of the organism, age, pathways, and others) in nature.

The numerous points that have to be taken into account when regulating a given substance determine the need to apply the principle of a limiting indicator. The principle requires that regulations be carried out on the basis of the most sensitive indicator. Thus, for instance, if the odour of a substance is perceived in concentrations that do not have a noxious effect on man and the environment, then regulations are based on the olfactory threshold. If the substance produces a harmful effect on the environment in concentrations that are smaller than those that could affect man, the threshold of its influence on the environment serves as a guideline for regulations.

The distinct nature of the hygienic assessment of atmospheric pollutants is also conditioned by their extreme variability in time and space which is due to various causes: unequal consumption of fuel, different intensity of road traffic, the nature of a technological process, methods of utilization of different substances (periodic use of pesticides), different efficiency and reliability of gas purification systems, etc.

Concentrations are heavily influenced by meteorological conditions that determine their transfer and dispersion in the air. The possibility of a sharp increase in concentrations is especially great during temperature inversions. If the inversion layer is situated above the stack, and air is intermixed below that level, this creates conditions for a rapid descend of the emission stream towards the earth's surface. The anticyclonic weather, characterized by very weak winds, calm, and descending air currents (especially in autumn and winter), may produce a stable layer of deep inversion above the stack.

With an inversion layer above the stack, the maximum ground-level concentration, which is possible under normal conditions, may increase two-fold. Under especially unfavourable conditions, when an inversion layer of several hundreds of meters and with a mean temperature gradient of 3 to 4°C per 100 meters forming above the stack, concentrations may be 5 to 10 or 20 times higher than the normal maximum concentration (M.E.Berlyand, 1975).

This list of causes of drastic changes in surface concentrations by no means exhausts the diversity of their variability. The constant modification of concentrations is due to constant changes in the direction of winds and their force. This explains the substantial differences between concentrations measured in the same point but at different times and under different conditions. That was why, when V.A.Ryazanov (1952) was formulating the basic principles of regulating atmospheric pollutants, he pointed out the necessity of using the term "concentration" with the indication of the period for which the analytical data were obtained: momentary, average values for 24 hours, average monthly values, etc. Hence, the normative values - MACs - should be different in terms of time. As the effect of a noxious substance varies both with its concentration and the duration of exposure, concentrations which are safe if inhaled over a short period may prove dangerous over a more prolonged period of inhalation. For substances possessing a general toxic effect with a marked cumulative impact, the MACs should be formulated in the light of the prolonged periods of their measurement (24 hours, a month, a year).

Due to substantial variability of the content of substances in the air, the average concentration over a long period is no guarantee that the amount of the substance during a short period will not exceed the acute impact threshold. Therefore, the average concentrations should be supplemented by the limits of their fluctuations, i.e. the maximum allowable single or "peak" concentration. This should first of all apply to substances with a pronounced irritating effect on mucous membranes and substances possessing a strong odour since no prolonged exposure is needed for the perception of the odour or irritation of mucous membranes.

It follows that for every substance polluting the atmospheric air it is necessary to establish short-term MACs to prevent reflex reactions of man (perception of odour, changes in the brain's bioelectrical activity and the eye's sensitivity to light, etc.) and long-term MACs to prevent the resorptive effect (general toxic, carcenogenic, mutagenic, etc.).

Concentrations whose cummulative frequency is equal to 70 per cent often correlate with the mean arithmetic concentration over the period of observation (e.g. a year). Therefore, the average yearly concentration as a mean arithmetic value is based virtually on single concentrations part of which (up to 70 per cent) are lower and part (up to 30 per cent) higher than the mean concentration. That is why an assessment of the degree of air pollution should take into account not only absolute values but the probability of their occurrence as well. Hence the need to regulate the probability of concentrations which are the same or lower than single MACs (M.A.Pinigin, 1979).

It was in the light of the above that the following definition of an MAC was formulated: "The maximum allowable concentration of a noxious substance in the air is a maximum concentration which is related to a certain mean period (30 minutes, 24 hours, a month, a year) and which, at a regulated probability of its occurrence, does not produce a direct or indirect harmful effect on man and his progeny, or lower his capacity for work, or affect his physical well-being".

2. ASSESSMENT OF AIR POLLUTANTS IN TERMS OF THEIR EFFECT ON HUMAN REFLEXES

A peculiar aspect of the assessment of the biological effect of air pollutants is primarily the study of their impact on man's sensory functions.

As the studies of air pollutants' effect on reflexes progressed, it became clear that their subsensory (non-identifiable by odour) concentrations are not indifferent for man and may, over a short period of inhalation, generate functional changes in man's mechanism of vision and the cortex.

These changes, which are a response to the impact of concentrations lower than the threshold concentrations in terms of odour, were used to substantiate single MACs for many air pollutants.

However, the elaboration of formulas using a certain coefficient that ensures a transfer from the threshold of the odour to the one-time MAC, made it necessary to develop a theoretical basis for determining safety factors. In this respect, attempts were made to apply a probabilistic approach to the determination of the threshold of an indefinite odour of substances. Dr. Andreyesheva's analysis of the results of determining theshold and ineffective concentrations of different substances showed that it would be adviseable to use the method of sampling to establish threshold concentrations. It was also established that the curves of "concentration - effect", in terms of olfactory reactions, had different inclinations on the probabilistic grid. This enabled the researchers to tackle the classification of substances' hazard in terms of olfactory reactions.

A scale of differentiated safety factors has been developed in accordance with the proposed classification of air pollutants in terms of the olfactory reactions provoked by them. This is undoubtedly only the beginning of the utilization of the probabilistic approach to the assessment of air pollutants' effect on man's olfactory system. Its continued application will ensure a more substantiated approach to the determination of single MACs (20 to 30 minutes), to the assessment of the substances' combined effect, and the degree of actual pollution of the air, taking into account human olfactory reactions.

Studies of the ties existing between human olfactory reactions, and the physical and chemical properties and the structure of the substance, deserve special attention. In particular, a certain interdependence was identified between the perception threshold of the odour of benzene derivatives and the nature and number of substituted groups. (Dr. Andreyesheva, 1978).

Therefore, the study of the influence of air pollutants on human olfactory functions has determined the peculiarities of the toxicological research therein. However, studies of the resorptive (general toxic) effect of the chemical agents that pollute the air also possess some peculiar features compared to the study of the resorptive effect of substances used in industrial toxicology.

3. PECULIARITIES OF TOXICOLOGICAL ASSESSMENT OF AIR POLLUTANTS IN TERMS OF THE RESORPTIVE EFFECT

Studies of the resorptive effect of substances that pollute the air are distinguished by the fact that their impact on the organism is assessed through the most sensitive methods: determination of threshold concentrations on the basis of "safe" concentrations, and chronic experiments with animals using continuous (3 to 4 months) inhalation poisoning because in human settlements man may be exposed to the continuous impact of air pollutants.

Different physiological, biochemical, histochemical, morphological and other indicators are used as criteria of the biological effect of air pollutants in these tests. Moreover, the threshold concentrations are believed to be minimal concentrations that produce changes in the functional condition of the organism and its vital organs and systems that go beyond the limits of their normal physiological fluctuations as evidenced by data on the original state of test animals and the control group.

Much importance is attached to chronic changes in the higher nervous activity of animals produced by inhalation of toxic substances. To assess the functional state of the cortex the Soviet hygienists and experts on communal toxicology resort to studies of the conditioned reflex activity, the interrelations between antagonistic muscles, and the latent reflex time. Some experiments are devoted to studies of the cholinesterase activity and of other enzymes, the ratio of protein fractions and the amount of the SH group in blood, the content of vitamins C, B_I and B_2 in organs and tissues, excretion of coproporphyrin, and many other highly sensitive indicators. The accumulated material shows that a prolonged exposure to small concentrations of air pollutants results in non-specific changes in the central nervous system, the blood system, the enzyme system, the vitamin system, and so on. However, in recent years, methods that demonstrate embryotoxic, gonadotoxic, allergenic, blastomogenic and other specific effects of chemical pollutants have gained much currency.

Thus, in recent years, there have been researches in the toxicometrics of air pollutants. The toxicometrics of air pollutants is based on researches in the nature of the interdependence between the time that certain toxic effects make themselves felt and the level of continuously inhaled concentrations, i.e. the concentration - time interdependence (M.A.Pinigin, 1976).

The research showed that continuous inhalation of different substances (acroleine, benzene and its homologues, carbon oxide, sulphuric gas, nitrogen dioxide, ozone and others) produces a "concentration - time" relationship, both in terms of acute chronic effects (lateral position, mortality of animals) and physiological, biochemical and pathomorphological changes (the reverse ratio of chronaxies of antagonistic muscles, the aggregate threshold indicator, the activity of cholinesterase of the whole blood, methemoglobinemia, carbooxigemoglobinemia, leukopenia, thrombocytopenic purpura, reticulocytosis, lower consumption of oxygen, sensibilization of the organism, vascular and distrophic modifications of the tissues, etc.) in the form of a hyperbole which on a logarithmic grid could be approximately represented by lines of different inclinations.

In accordance with the equation of the line $y=AX-B$, the empirical expression of the "concentration - time" dependence can be written in the general way: $\lg C = \lg C_0 - \operatorname{tg}\alpha \cdot \lg T$, where C is a concentration which produces a toxic effect within time T; C_0 - a concentration which produces the same effect within the time equal to the adopted time unit (an hour, 24 hours); α - angle of inclination of the line towards the abscisa. Since the line goes upwards and to the left, the angle of inclination lies between 90° and 180°.

Since the "concentration - time" curves are an integral reflection of the toxicodynamics of a substance and the organism's ability to offset its effect, the parameters of these curves (the angle of inclination and the tangent of the angle) make it possible to determine the hazard of the substance: the greater the tangent of the angle, or the smaller the angle, the less dangerous the substance is, since the duration of the period during which the effect is felt increases significantly.

The above classification characterizes substances in terms of the danger of chronic intoxication, and, all other conditions being equal, shows that the more dangerous the substance is the lower the threshold of its chronic effect. The comparisons undertaken demonstrated that the class of hazard of a substance established for continuous inhalation remains unchanged for its intermittent inhalation. This made it possible to include in the list of MACs for atmospheric pollutants the classes of hazard corresponding to the classes adopted for the same pollutants (substances) in industrial toxicology.

Since under real conditions there may sometimes be a sharp increase in the concentrations of air pollutants and a danger of acute unfavourable effects (e.g. and irritating effect, exacerbation of a chronic disease, etc.), this generates the need to classify these substances in terms of a danger of man's acute reactions provoked unuer their impact. In this case, the above classification is replaced by its opposite.

The classification of the substances' hazard in terms of the "concentration - time" curves was also used to substantiate the scale of "safety factors" used to establish average yearly MACs. The lowest safety factor of "5" is situated on the border of moderately and highly hazard substances (the angle of inclination of the "concentration - time" curve is 137°). Starting from this point the values of the safety factor go up to and over 25 since there is an increase in the danger of chronic effects, on the one hand, and acute effects, on the other. A special nomogram makes it possible to determine more differentiated safety factors.

The basics of the toxicology of air pollutants with a continuous effect elaborated in recent years made it possible to suggest an accelerated method of determining MACs for different chemical agents.

Thus, the average yearly MAC is determined on the basis of the results of a chronic animal experiment. The allowable frequency of concentrations at the level and below a single MAC is determined on the basis of this concentration and the value of a single MAC (20 to 30 minutes). In practice, to establish a single MAC for a given substance at the level higher than its average yearly MAC means to allow the occurrence of a single concentration which is higher than the average yearly MAC, the difference being equal to the ratio between the single MAC and the average yearly MAC of the substance. For example, in the case of benzene, the ratio is 1:15, sulphuric gas - 1:10, and nitrogen dioxide - 1:2.1.

The existence of single MACs, that are higher than average yearly MACs, raises the need to establish allowable frequencies of concentrations at the level, and below, single MACs. Without this limitation the existence of concentrations at the level of a single MAC over a prolonged period will result in the level of an average concentration over this period that might exceed the level of the average 24-hour MAC, and, consequently, in a danger of resorptive effects in the absence of the danger of reflex reactions.

It follows from the above that the allowable frequency of concentrations at the level of single MACs regulated on the basis of reflex reactions, must be introduced in order to prevent resorptive effects produced by a prolonged impact of a substance. Our research has shown that the allowable frequency of concentrations should be determined with account taken of not only intermittent (discrete) action but continuous action as well, when concentrations equal to a single concentration will exist during a certain period of time. It was established that in the case of a continuous action the frequency of concentrations at the level of a single MAC, and higher, is limited by the peculiarities of substances belonging to Class IV of hazard since they create the highest danger of acute effects, and in the case of discrete action - the peculiarities of action of the substances of Class I of hazard that have marked cumulative properties. For the practical purposes of determining the admissible frequency of concentrations at the level of single MACs, a special scale was suggested which regulates this value in accordance with the ratio between a single and the average 24-hour MAC, determined for a given substance in accordance with its reflex and resorptive effects. For example, with the ratio between these concentrations equal to 1:10, the admissible frequency of concentrations at the level of a single MAC, and higher, should not exceed I per cent.

To determine the allowable frequency of concentrations at the level of a single MAC, and higher, use was made of the results of research in the resorptive effect of substances during discrete and continuous inhalation.

M.T. Dmitriev

METHODS OF AIR AND WATER CHEMICAL ANALYSIS IN COMMUNAL TOXICOLOGY

Current problems of communal toxicology cannot be solved without carrying out effective studies on the chemistry of atmosphere, water bodies and other components of the environment. Such research is primarily required to obtain comprehensive information on the quality of the environment and the progresses occurring in air and water. The principal objectives of investigation in communal toxicology are: to elaborate adequate and accurate methods of chemical research, to develop a theory of the chemical progress in the environment, and to solve physico-chemical hygienic problems. It is also necessary to work out new and improve the presently available sanitary-chemical methods of toxicant determination to be used not only in scientific research but also by medical colleges, epidemiological stations, hydrometereorological service, and hydienic chemistry laboratories at industrial enterprises. The tasks of chemists working in communal toxicology also involve direct hygienic studies (G.I.Sidorenko; M.T.Dmitriev, 2976).

The urgency of these problems can be exemplified by the control over environment pollution in the areas occupied by modern industrial complexes releasing scores and even hundreds of various toxic substances into the environment. Consequently, the most significant results in this field have been obtained in elaborating the chemical methods with the use of gas chromatography, mass spectrometry, chromato-mass spectrometry, spectrophotometry, polarography, chemiluminescence, radioactive isotopes, and X-ray fluorescence in particular. In developing gas chromatographic methods of analysis emphasis is being placed on simultaneous highly sensitive and separate determination of numerous toxic compounds, belonging to the same class and having similar physico-chemical properties, against the background of a complex "bouquet" of associated substances. Conventional methods used for a chemical analysis of complex mixtures of toxic substances are nonselective.

Gas chromatography finds an ever increasing use in the analysis of both air and water. The main advantage of this methods is the possibility of separating a mixture of substances into individual compounds. Of great importance is the fact that analysis can be performed relatively fast. The logarithm of retention volume for most substances is approximately proportional to the ratio between the boiling temperature and the temperature of the column, expressed in adsolute degree. To determine the sensitivity of the analysis it is convenient to use the ratios between the degrees of ionization of substances, when these ratios are similar for different classes of substances and chromatograph detectors. For carbonyl compounds the degree of ionisation rises sharply with an increase in the number of carbon atoms, while for all hydrocarbons it is a value of the same order of magnitude and is close to $3\cdot 19\cdot 10^{-8}$ K/μg.

Of great importance is the method of sampling for gas-chromatographic determination of toxic substances in the atmospheric air or in the air of residential and public buildings, since sample collection entails the concentration of toxicants. Methods have been elaborated to collect samples into cooled and uncooled tubes on polymeric sorbents and into absorbers with porous membranes, followed by introducing the liquid samples into a chromatograph (M.I.Dmitriev, V.A.Mishtchikhin, 1980). Some of the methods are not devoid of disadvantage (as applied to certain specific conditions) and, therefore, find only a limited application. For instance, when liquid solutions (from absorbers) are introduced into a chromatograph in the amount of no more than 1-5 µl, the main part of the sample is lost (with larger samples gas-chromatographic separation is impossible). This method is only effective for the substances with sufficiently high MAC (of the order of 0.05-0.5 mg/m^3, depending on the chromatograph sensitivity). The procedure cannot be widely applied to take samples in the field when use is made of cooling agents, such as liquified gases, dry ice or liquid mixtures. Moreover, such sampling technique requires preliminary drying of samples and, therefore, selection of optimal drying agents.

Most effective is the direct sample collection into uncooled tubes. If, however, they are filled only with a conventional stationary phase, sensitivity of the subsequent gas-chromatographic determination may prove insufficient. To considerably extend the list of substances whose gas-chromatographic analysis can be performed with samples collected into uncooled tubes, a method has been developed of concentrating the samples on low-polar polymeric porous sorbents. The specific surface of a typical hydrophobic sorbent of this type - polysorb I (copolymer of styrene with divinyl benzene) amounts to 200-250 m^2/g, while that of firebrick or chromosord does not exceed 4-8 m^2/g. The time to determine the retention volume can be significantly reduced if the measurements are made at high temperature. The obtained retention volume values (reaching 2 m^3 for decane) show that field sampling can be performed with the help of polymeric sorbents without any cooling agents. The time of storing the collected samples in sampling tubes is virtually unlimited.

Addition of liquified gasses to the samples, already absorbed in the tubes, to be analyzed in the laboratory raises considerably the separation efficiency when a condenser is used. Direct connection of the tube with polymeric sorbents to the gas chromatopraph results in a considerable blurring of chromatographic peaks, caused by a substantial increase of the elution time owing to large specific surface of sorbents. Chromatographic separation is most effective if the surface of the stationary phase is not expanded at all in addition to the gas-chromatographic column, i.e. when the sample tube with a porous sorbent is replaced by an unfilled one (condenser). The substances to be determined are transferred into the cooled condenser with the help of a carrier gas, electrical oven, and feeder cock. Complete desorption of the substances into the condenser at the carrier gas flow rate of 0.1 1/min takes place within 20-25 minutes. The use of the condenser results in a complete separation of the substances, characteristic of a given chromatographic column.

Naturally, if the chromatograph sensitivity is high enough, the collection of samples into uncooled tubes with a conventional phase or into absorbers fitted with a porous membrane can also be optimal, which makes it possible to dispense with cooling mixtures altogether. Sampling into liquid solutions also has some advantages, since in this case the chromatogram is not affected by oxygen, methane, condensed water vapours, or carbon dioxide. Gas-chromatografic methods are also effective in determining individual substances in complex mixtures, when their identification and analysis are of paramount hygienic significance. Typical examples of such applifications include the development of methods to determine hydrocyanic acid, dioyane, tetraethyl lead, nitric oxide, methanol, vinyl chloride, phenol, carbon monoxide, carbon disulfide, nicotine, caffeine, and other substances.

In addition to gas-chromatography, also quite effective are paper,thin-layer and liquid chromatography. The chromatographic analysis efficiency can be appreciably raised if it is preceded by performing the chemical reactions specific for the group of compounds to be determined (I.A.Pinigina, 1980). Intensive research has also been carried out in the field of mass spectrometry and chromato-mass spectrometry of environmental pollutants. Mass spectrometry is one of the most advanced and universal types of the present-day physico-chemical analysis. Among the main advantages of the method are its high specificity and sentivity, a possibility of direct identification of unknown compounds, and automatic recording of the data obtained (B.I.Keda, 1981).

Spectrophotometric methods of investigation are also of great scientific and practical importance, as they make it possible to obtain information on the structure of molecules, the mechanism and rate of analytical chemical reactions, and, therefore, on the content of toxic substances in the analyzed samples. The most effective is spectrophotometry based on the absorption of electromagnetic radiation. The resolving power and informative value of the spectra depend to a considerable extent on the energy range or radiation wavelengths, the properties of determined compounds and the physico-chemical processes taking place. When radiation is absorbed in the ultraviolet and visible regions, the absorption is mainly due to the electron excitation of the outer shells of atoms and molecules. Infrared radiation excites the vibrational levels of molecules. Radiation absorption in the microwave and radiowave regions leads to the excitation of the rotational levels of molecules, to an increase in the energy levels of nuclear and electron spins, thereby enabling the NMR and the EPR spectra to be obtained. Spectrometric methods are effective in determining the main inorganic air and water pollutants.

Considerable possibilities are offered by the chemiluminescence methods. With the help of chemiluminescence are effectively determined: nitric oxide and dioxide (after converted into oxide), ozone(by its reaction with ethylene), and many other substances. The use of a gas-chromatographic column and a chemiluminescent detector with ozone enable the detection of an unlimited number of unsaturated organic compounds reacting with ozone. The use of gas chromatography raises considerably the analysis specificity. The interfering action of associated substances can in this case be completely disregarded. At the same time, the sensitivity of a chemiluminescent chromatograph is 10^3-10^6 times higher than that of a chromatograph with a flame-ionization detector. That is why the use of the chemiluminescent chromatograph makes it possible to determine most of the inorganic substances at concentrations significantly lower than MAC, without any preliminary condensation of samples. This, in its turn, increases appreciably not only the sensitivity but also the accuracy and the rapidity of analysis.

Radiological methods of investigation are also very promising. With the help of radioactive indicators one can unambioguously establish the distribution of toxic substances in the organism of experimental animals, to follow up the transport and localization of these chemicals (O.I.Yurasova et al., 1980). The use of radioactive isotopes and radiation also raises substantially the specifity of physico-chemical analysis and increases considerably its sensitivity. Thus, an increase in the ionization level of the tested sample in the detectors of gas chromatographs using radioactive sources (electron-capture, argon or helium-ionisation detectors, etc.) raises considerably the sensitivity and specificity of determinations. Some radiological techniques, e.g. the method of neuron activation analysis, are up to now considered to be unsurpassed in sensitivity and reliability. Special reference should be made to the highly promising fluorescent X-ray - radiometric determination of heavy matals, since this method is based on using radioisotope sources with a very low activity and readily available portable apparatus.

Of great importance in communal toxicology is the designing of the equipment used to analyze atmospheric air, air medium of premises, and water. Thus, the chemical luminescence analyser of ozone in air, using the reaction with ethylene, has a higher sensitivity and specificity as compared with all the existing ozone analyzers. A portable automatic ozone analyzer where rhodamine C is used as chemiluminophore has a sensitivity of 5 $\mu g/m^3$ and weighs not more than 4 kg. The sensitivity of the method increases 40-70-fold if ozone reacts with rhodamine activated with gum arabic. The interfering action of nitrogen oxides does not exceed 0.05-0.15 per cent. The principal purpose of the portable analyzer is to control the ozone content in the atmospheric air and in aircraft cabins. The coulometric ozone analyzer (with sodium bromide used as electrolyte) has an insignificant background current, sensitivity of analysis is of the order of 1 $\mu g/m^3$. Ozone concentration is directly proportional to the electric current induced in the coulometric cell. When a cylinder with oxygen (instead of one with ethylene) and a calibrated ozonizer are connected to the chemiluminescent ozone analyzer (using the reaction with ethylene) the instrument serves as an automatic analyzer for nitric oxide. If the instrument is additionally equipped with a converter of nitric dioxide into nitric oxide, it can simultaneously determine the sum total of nitrogen oxides. The chemiluminescent analyzer is also used as the detector in a chemiluminescent chromatograph. A portable instrument has been developed for the determination of total organic substances in air, based on a flame-ionization detector and air purification device. If the chromatograph is equipped with a methanator (converter of carbon monoxide into methane), it can be used as a highly sensitive and specific analyzer of carbon monoxide in air. Determination sensitivity amounts to 0.05 mg/m^3. A gas analyzer and an automatic station for integrated investigations of the state of air medium and indoor air exchange have been designed, based on infrared-photometric determination of carbon dioxide. A diffusion of preset concentrations in the range of 0.01-1.0 mg/m^3 and higher has been developed and successfully used in hygienic investigations, along with devices for the sampling of atmospheric air followed by its concentration, and for the concentration of toxic substances from water.

Along with specific determination of individual substances, of great methodological importance is also the development of group indicators or indices of overall environmental pollution, and of methods for their measurement. The use of mass spectrometry and chromato-mass spectrometry for the analysis of toxic substances in air water shows that in many cases the environment is simultaneously polluted with scores and even hundreds of toxic substances of approximately equal hygienic significance. At the same time, the data of such analyses are not infrequently used only for subsequent calculation of the overall and the hypothetical pollution indices. It has been found that the same data can be also obtained by means of rapid determination of an overall pollution index, since a clear-cut correlation is usually traced between them (Yu.D.Gubernsky, M.T.Dmitriev, 1981). A number of such overall indices have been suggested recently. Characteristic aspects of their application and determination can be examined in detail as exemplified by one of them - the ozone index, serving as an overall indicator of air pollution.

Ozone is known to degrade intensively in the air, oxidizing the majority of inorganic pollutants: ammonia, nitric oxide, sulfur dioxide, hydrogen sulfide, aldehydes, alcohols, amines, mercaptanes and numerous hydrocarbons. Ozone disentegration in the course of its interaction with all the pollutants mainly follows the scheme of bimolecular reaction. Since the overwhelming majority of the rate constants of reactions between diverse pollutants and ozone are unknown, it is desirable that the value of the ozone index be expressed in terms of only one substance, for which this rate constant has been determined with high accuracy. Moreover, it is important that this substance should be widely occuring convenient to handle in experiments, and also be contained in the air as a pollutant among other substances. Hexene-1 was selected as such a substance; the rate constant of its reaction with ozone is $5.96 \cdot 10^6$ $cm^3/mole.s$ (which corresponds to $1.19 \cdot 10^{-2}$ $m/mg.min$). The ozone pollution index thus reflects the overall concentration of all the pollutants in the tested air sample by their reaction with ozone in terms of hexene. Since all the substances reacting with ozone in the air are pollutants, the ozone pollution index directly characterizes the purity of air: the lower the index, the less the pollution. Expressed numerically, the ozone index is equal to the calculated hexene concentration which would lead to the same rate of ozone disentegration as the total number of pollutants contained in it. Experimental determination of the ozone does not present any difficulties, since it is only necessary for this purpose to have an ozonizer and a device or a method to measure the ozone concentration. The optimal duration of the ozone index determination is 15 minutes. The value of the ozone index also makes it possible to obtain the overall of the hypothetical pollution indices.

Along with the ozone index, other group indicators of air pollution have been developed: the total content of organic carbon and photooxidants, the nitric oxide oxidation rate, the carbonyl, ionic and chemiluminescent indices. The total content of organic carbon is directly determined with the help of a gas chromatograph having a flame-ionization detector and characterizes air pollution, primarily with hydrocarbons. The total content of photooxidants simultaneously characterized air pollution with nitrogen oxides and hydrocarbons, as well as the intensity of photochemical reactions. The nitric oxide oxidation rate is an indicator of the development of photochemical reactions, particularly of the moment of a sharp rise in ozone content. The carbonyl index shows that the air contains the products of incomplete fuel combustion. The ionic index (the ratio between the concentrations of heavy and light ions)reflects the overall air pollution, while the chemiluminescent index - the total content of unsaturated compounds, nitrogen oxides or products of photochemical reactions. The application of organoleptic indicators of air pollution is effective in some cases. The use of group indicators is also expedient in water analysis. Oxidizability is the best known of these indicators. The index of total organic carbon content is usually determined to assess organic pollution of water with the help of a gas chromatograph or a portable analyzer. The use of the ozone index is also quite promising for the integrated water analysis. As in the case of air, determination of individual substances is important for water analysis as well (Yu.V.Novikov, et al., 1981).

Low-temperature fluorescent spectral analysis has been successfully applied to determine polycyclic aromatic hydrocarbons: benz(a)-pyrene, 1,2-benzanthracene, and 1,12-benzpyrilene. When frozen to the temperature of liquid nitrogen, solutions of polycyclic aromatic hydrocarbons in normal paraffins have quasi-linear fluorescence spectra, specific for individual substances and closely approximating the atomic spectra. Therefore, the method is not only highly sensitive (its sensitivity is of the order of 0.1 ng/ml) but also highly specific. The advantage of atomic-absorption analysis lies in its high sensitivity, selectivity, rapidity, and accuracy. The application of nonflame atomization methods, graphite cells with a temperature of 2500-2600° in particular, makes it possible to increase substantially the sensitivity of the analysis. Lead, cadmium, manganese, nickel, calcium, magnesium and many other heavy metals are determined in water by means of atomic-absorption spectrophotometry.

Precise determination of trace metals can be also performed with the help of neutron activation analysis. Test samples are exposed to neutron radiation in portable neutron multipliers or in nuclear reactors, with nuclear reactions resulting in the formation of radioactive isotopes. Comparing the ratioactivity of samples with standards one can determine the content of analyzed metals with a sensitivity reaching 0.1-1.0 pg. An instrumental method of neutron activation is used to determine aluminum, barium, calcium, chlorine, potassium, magnesium, sodium, strontium, and vanadium. Neuron activation method with radiochemical separation, using diethyl dithiocarbamates of different metals, is more effective to determine copper, molybdenum, cobalt, iron, zinc, and arsenic. Chromato-mass spectrometry is the most up-to-date method of unique potentialities. It is effectively used to analyze chlorinated hydrocarbons, aromatic compounds, naphthenes, terpenes, and other substances in water. Thus, the present-day methods of chemical analysis make it possible to control air and water pollution with high sensitivity, reliability and rapidity.

REFERENCES

Gubernsky, Yu.D., Dmitriev, M.T. Teoria i praktika fisitcheskoi kultury, 1981, No 1. p.17.

Dmitriev, M.T. Atomnaya energia, 1965, vol. 19, No 1, p. 97.

Dmitriev, M.T., Mishtchikhin, V.A. Gigiena i sanitaria, 1980. No 9, p.66.

Keda, B.I. Khimia za rubezhom (Chemistry Abroad), Moscow, 1981, p. 63.

Novikov, Yu.V., Latotchkina, K.O., Boldina, Z.N. Metody opredeleniya vrednych vestchestv v vode vodoyomov, (Methods for Determination of Harmful Substances in Water). Moscow, 1981.

Pinigina, I.A. In: Phisico-khimitcheskie metody issledovaniya okruzhayushtchey sredy (Physico-Chemical Methods for Environmental Studies). Moscow, 1980, p.24.

Sidorenko, G.I., Dmitriev, M.T. In: Unifitsirovanie metody opredeleniya atmosphernych zagryazneniy (Standard Methods of Air Pollution Determination), Moscow, 1976, p. 9.

Yurasova, O.I. et al. Gigiena i sanitaria, 1980, No 2, p. 54.

TOXICITY ASSESSMENT OF HOUSEHOLD CHEMICALS

S.I.Voloshchenko

Household chemicals (HC) are widely used throughout the world.

Functionally HC can be subdivided as follows:

I. Detergents

1. Synthetic detergents
2. Heavy duty detergents and water softeners
3. Bleaching, blueing and starching agents
4. Shampoos
5. Bath shampoos
6. Heavy duty detergents to remove dirt from heavily soiled hands, vehicles, etc.

II. Cleaning agents

1. Cleaning agents for kitchen utensils.
2. Carpet and rug cleaners
3. Glass, ceramics and china cleaners
4. Cleaning agents for precious metals, copper etc.

III. Stain removers

IV. Polishes

1. Furniture polishes
2. Floor polishes
3. Car polishes

V. Toiletries

1. Hair sprays
2. Deodorants

VI. Adhesive agents (glues, sealants, putty)

VII. Paints and varnishes (varnishes, paints, solvents)

VIII. Leather and chamois care articles

IX. Household aerosols

X. Insecticides and pesticides

XI. Herbicides

XII . Photo-chemicals

XIII. Mineral fertilizers

XIV. Other household chemicals (plasticine, ski wax, candles, dyes, coniferous bath extracts)

Synthetic detergents (SD) account for a major portion of HC. Surface active substances (SAS) and synthetic detergents are basically treated as possessing mild toxic properties. Their median lethal doses for white rats range from 1.500 to 20.000 mg/kg applied perorally and 2.500 - 40.000 and more mg/kg if applied cutaneously. (O.I.Voloshchenko, et al., 1977; V.A.Pokrovsky et al., 1975, etc.).

Cases of poisoning at home with household chemicals have been described in the literature. (I.P.Zamotayev et al., 1978, etc.)

Analysis of questionnaires circulated among the citizens suggests that the use of a powdered synthetic detergent for household needs may result in contamination of the ambient air with SD aerosols. We have ascertained a brief presence of detergents in the air of non-living quarters in apartments where synthetic detergents have been used. The maximum content of anion surface active substances (SAS) in the air did not exceed 0.12 mg/m^3. Migration of surface active substances in the air space of living quarters depends on the microclimate. Air circulation and relative humidity bring down surfactants' concentration in the air space of the living quarters. (O.I.Voloshchenko et al., 1979).

We have ascertained the presence of anion SAS on the walls, floor and bathroom fixtures following the use of SD, their amount not exceeding 0.4 μg/sq cm. Residual SAS up to 9 μg/sq cm. on the skin of human hands were determined following contact with the water solution of detergents (O.I.Voloshchenko et al., 1979) Z.S.Markova and A.I.Sautin (1979) have established a direct relationship between the residual detergents on the skin of the hands and the SD concentration, temperature and exposure time.

The latent danger inherent in the use of household chemicals (HC) packed in pressurized cans lies in the possibility of poisonous substances' arriving into the human body perorally or through the skin and the mucous membranes.

People may be exposed to detergents in their own homes, but also as a result of environmental pollution. We believe (O.I.Voloshchenko, 1979, 1981) that in the context of the wide use of detergents for household needs the predominant pathway for SAS and other components of synthetic washing powders is through the skin. Degreased skin is particularly susceptible to dermatitis that develops in persons whose skin is overly sensitive to chemicals, including detergents. An important factor here is represented by the time lipids take to regenerate and the active skin reaction (pH) takes to return back to normal following exposure of the skin of the hands to household solution of SD. Apart from degreasing SAS's cause denaturation of the skin. Changes have been identified in the skin microcirculatory systems, and disruption in the cellular ultrastructure and intercellular contact structure.

Despite the fact that in the present-day household the skin is the main pathway into the human body for SAS, and mindful of the wide use of detergents in many households, even though on a very small scale, cognisant of the possibility that they may find their way into drinking water and food we could reasonably suppose that people may be wide open to an intricate integrated and combined impact of the detergents' basic components on the human body. In the future study, this problem will be both urgent and appropriate in the hygiene and toxicology of household chemicals (O.I.Voloshchenko et al., 1981, I.V.Mudry, 1980).

THE PROGRAMME FOR THE TOXICOLOGICAL AND HYGIENIC STUDY OF HOUSEHOLD CHEMICALS

Depending on the formula of a household chemical and mode for its application the study of a possible adverse impact on the human body involves application to the skin, introduction into the stomach or inhalation by test animals of a preparation diluted to recommended concentration.

Since household chemical affect in one way or another most people, doses and concentrations of experimental chemicals exceed the recommended doses and concentrations by a factor of 2-4, to ensure a safety margin. In short term experiments lethal doses and median lethal doses for test animals are determined following a one-time exposure to the chemicals in question, which are introduced into the body in different ways. The animals are monitored for overall condition and body weight for 2 weeks. The control animals are exposed to the solvent internally or by external application.

It is recommended that the cumulative properties of chemical preparations should be studied involving the same type of test animals as ones used for the acute experiment. The cumulation coefficient is calculated from one of the methods developed by U.S. Kagan, 1974, G.N.Krasovsky, 1977 and others.

In staging a chronic toxicological experiment it is expedient to recommend a number of biochemical, physiological, histological, radiological and hematological research techniques.

Taking account of the hygienic importance of skin exposure to SAS the research programme should include the study of skin permeability to major detergents.

To predict a possible adverse effect of synthetic detergents on the human body it would be advisable both to look into their allergenic, mutagenic, carcinogenic, teratogenic effects and to simultaneously study the functional condition of the skin of hands at direct contact with detergents water solution.

HOW TO DETERMINE TOXICITY PARAMETERS FOR HOUSEHOLD CHEMICALS IN ACUTE EXPERIMENT INVOLVING DIFFERENT PATHWAYS

Information as to DL_{50} for SD and SAS is important both in scientific and practical terms. Median lethal doses and concentrations are necessary for incisive toxicological research into new chemicals (cumulative properties, tentative threshold doses, tentative safe exposure levels).

To arrive at DL_{50} different statistical data processing techniques have been put forward. (M.L.Belenky, 1963). More complete information related to parameters of substances' acute toxicity can be furnished by probit-analysis proposed by Leachfield and Wilcoxon. To arrive at DL_{50} of chemicals a technique proposed by B.B.Prozorovsky (1960) is also widely used.

An acute experiment is conducted by a one-time introduction of a household chemical into the body of a test animal through different pathways (cutaneous application, oral applications, inhalation).

The fundamental indicator for hazardous properties of chemicals affecting a living organism at high doses (or concentrations) is represented by the DL_{50} and its error. At the same time the need arises for the study of other parameters of acute toxicity $\frac{1}{DL_{50}{}^{s}}$; $\frac{DL_{84}}{DL_{16}}$; the function of the inclimation angle S (I.V.Sanotsky, N.P.Ulanova, 1975). To evaluate the combined and complex effect of surfactants on the human body the classical technique of Lõwe and Finni (1952) can be used, or the technique of Finni modified by Yu.S.Kagan (1973); V.I.Svatkova et al (1981) etc.

MATERIAL ACCUMULATION OF HOUSEHOLD CHEMICALS: DETECTION AND GRAVITY

The accumulation problem constitutes one of the most urgent ones in the present-day hygiene and toxicology. The environmental factors may have different impacts depending on their structure.

There are two methods to assess accumulation that are most widely used. One is based upon a regular (daily) introduction into the test animals of equal doses, representing a certain proportion of DL_{50}(L.I.Medved et al., 1968). The other technique known as the subchronic toxicity test is based upon a gradual increase of the preparation dose (Lim et al., 1981). In both cases the cumulation coefficient (K) can be calculated as the ratio:

$$\frac{\sum DL_{50}\ (n)}{DL_{50}\ (I)}$$

Anion and non-ionogenic SAS and SD incorporating them possess distinct cumulative properties. Synthetic detergents show a lower cumulative capability than surface active substances. For surface active substances and synthetic detergents the cumulation coefficient ranges between 5 and 6 plus.

METHODOLOGICAL APPROACHES TO THE ESTABLISHMENT OF THRESHOLD DOSES FOR HOUSEHOLD CHEMICALS INVOLVING THE ENTIRE SET OF TOXICOLOGICAL AND OTHER INDICATORS OF THE ORGANISM

The chronic sanitary and toxicological experiment must furnish an answer as to the nature of biological impacts and mechanism of action of household chemicals, which will make it possible to arrive at the threshold doses and concentrations.

Although each SAS is characterized by its own distinctions in interacting with the organism, it is possible to identify organs most vulnerable to these substances and synthetic washing powders utilizing them. The organs include the liver (O.I.Voloshchenko et al., 1977), the intestinal tract and stomach (T.V.Babadzhanova, 1966) form blood elements (Ya.V.Gamitkevitch, T.N.Bozheskova, 1975) and the nervous system. The impact of SAS and detergents may frequently result in hyperphospholipaemia, hyperholisterinaemia and other metabolism disturbances in the body of animals (O.I.Voloshchenko et al., 1981).

For the chronic experiment (6 months) the following indicators may be recommended for investigation.

- physiological indicators: the animals' capacity for work, summation threshold indicator, different tests characterising the higher nervous activity and behavioural responses of the animals, their ECG and EEG.

- hematological indicators (erythrocytes, leukocytes, haemoglobin)

- biochemical indicators: total albumin of blood serum, physicochemical properties of blood albumins in terms of specific weight, albumin fractions of blood serum, temperature resistance of blood serum albumins, albumin in urine, urea in blood and urine, cholesterol in blood serum, total blood lipids from the gravidimetric technique, - lipoproteides, free and total cholesterol in the liver (the Sperry - Web technique), glucose in blood, glycogen in the liver, pyroracemic and lactic acid, choline esterase, catalase and peroxidase of the blood, succinate dehydrogenase, alkaline phosphatase, transaminase of the blood serum, etc.

By the harmful exposure on the animal body the threshold doses of anion and non-ionogenic surface active substances range, in the case of cutaneous applications, from 10 to 100 mg/kg; synthetic detergents - from 20 to 100 mg/kg and more (O.I.Voloshchenko et al., 1981).

A certain measure of importance in characterising the adverse effect of surface active substances and synthetic detergents is attached to the chronic exposure zone determined from the ratio of the acute over chronic exposure threshold. The wider the zone, the more hazardous the substance, because there is a possibility of chronic poisoning at low doses.

To establish Lim_{ch} the results of the chronic experiment should be statistically processed using Student's criterion. The integrated and combined effects of the surface active substances on the body can be assessed using the technique of Z.D. Zlatyev et al. (1977), Z.Z.Bruskina (1978), L.A.Timofeyevskaya N.N., Melnikova (1980), V.I.Svatkov et al. (1981).

Major attention is given to the testing of household chemicals under natural conditions, i.e. in the course of 20-minute long contact between the skin of human hands and water solution of the detergents. In this study, one of the most important factors is skin degreasing, pH and total aminoacids on the skin. The pH level after a 20-minute long hand-washing in a synthetic detergent must be back to normal 1-1.5 hours following the contact. The total lipids on the hands' skin usually go down 25-45 per cent as compared to the original level and 3 or 4 hours after recovery to the original level (O.I.Voloshchenko et al. (1977).

The concentration of total aminoacids on human hands is investigated for several days after the experimental exposure. It has been noticed that even 72 hours after contact with a synthetic detergent the total aminoacids do not get back to the original level. The recovery level may range from 75 to 92%. Higher pH of the hands's skin and lower lipids and aminoacids on the skin of the palms and forearms result in deteriorated skin condition. To prevent dermatitis the recommended concentrations of detergents should not cause vigorous degreasing or higher active reaction of the skin. Cream for hands should be applied following contact with solutions of synthetic detergents.

ASSESSMENT AND DEGREE OF ALLERGENIC, MUTAGENIC, CARCINOGENIC AND TERATOGENIC EFFECT OF HOUSEHOLD CHEMICALS

(the Example of Synthetic Detergents)

Surface active substances and synthetic detergents may cause allergenic reactions if absorbed by the skin, thus promoting allergenic contact dermatites and general symptoms of allergy.

Surface active substances possess threshold allergic doses that are 2 to 3 times lower than the threshold toxic doses, and for synthetic detergents they range from 100 to 100 mg/kg.

Delayed effects of household chemicals impact can be grouped together in the following manner: embryotoxic and teratogenic impact, mutagenic impact and its implications for the offspring, possible carcinogenic effect on the organism.

Literature suggests that certain surface active substances (linear alkylbenzolesulphonate) if ingested, increase morbidity of test animals in embryo, (Palmer, 1975).

To give a hygienic characteristics of surface active substances and related household chemicals widely used for household purposes in the human environment in low or sublow amounts, information is necessary on their possible mutagenic effect on the organism.

The study of carcinogenic effect of surface active substances, detergents and other household chemicals is as important as the study of these substances' toxico-dynamic and sensitizing properties. Early detection of carcinogenic substances among household chemicals, synthetic detergents, etc. with a subsequent ban on their production, will have a major part to play in preventing malignant tumors.

Sulphanol NP-3 and Synthanol-DS-10 (35,36) have been described in the literature as promoting induced chemical carcinogenesis. (Yu.I.Sakharov et al., 1973, A.V.Sinigina, Yu.I.Sakharov, 1974).

Sulphanol chloride and primary sodium alkylsulphate did not experimentally prove to possess carcinogenic properties at concentrations or doses to which people are in fact exposed while using synthetic detergents in the express (sebaceous gland suppression) test or chronic experiments involving cutaneous application of the surface active substance on mice. At the same time, co-carcinogenic impact of sulphanol chloride has been established if it is cutaneously applied at a concentration which is by an order of magnitude higher than the actual concentration that can be observed under household conditions. (N.Ya.Yanysheva et al., 1982).

Therefore we should amplify the importance of studying possible delayed consequences of surface active substances and their impact on the human organism.

The last decade has seen increased production of detèrgents including proteolytic enzymes. Addition of enzymes to synthetic detergents make them more effective as washing preparations.

These chemicals do not affect the pH and lipids of the skin as drastically compared to enzymaless synthetic detergents. Detergents with enzymes have a negative effect on the human skin because instead of proteolytic enzymes they are made with a combination of different anion surface active substances and other components. In putting together new formulas, account must be taken of the proportion of anion and non-ionogenic surface active substances in the detergent, which may result in synergism or antagonism in the effect of detegrents belonging to different classes, not only in terms of their cleaning properties, but also in terms of their impact upon the skin's functional properties.

Having penetrated the body synthetic detergents may be deposited in certain organs and systems and play a role in the disbalance of the endogenic surface active substances in the organism's internal medium. The problem is of current interest and may have theoretical and practical significance.

TOXICITY AS THE NUMBER ONE CRITERION IN HYGIENIC RESTRICTIONS ON HOUSEHOLD CHEMICALS

The scientific and technological advancement has engendered a major challenge faced by preventive medicine, a task of studying the environmental factors for purposes of hygienic assessment, hygienic classification and standardization of raw materials and manufactured articles, hygiene-oriented restrictions or reductions in the intensity of adverse industrial or household impacts on the human body.

One marvels at the eternal truth of N.S.Pravdin's words, who said: "The scientific might ... of toxicology can be found in the triade of clinical, hygienic and experimental studies" (I.V.Sanotsky, I.N. Ulanova, 1975).

The toxicology of household chemicals is included as a section into general hygienic toxicology which studies the interaction of household chemicals with the organism of man and animals. Its fundamental task lies in establishing latent and overt hazards inherent in SAS, SD and other products used as household items and in various sectors of national economy.

Hazard represented by chemical preparations is not only understood as chemicals' capability to cause acute or chronic poisonings, but also as their selectivity in affecting organs and physiological systems, particular links in the metabolic chain, and to alter the body's reactive responses, blastomogenic, carcinogenic, embryotoxic, teratogenic and mutagenic properties of the factors in the environment (Yu.S.Kagan, 1981).

Therefore it can be safely stated that the establishment of toxicity represents the fundamental criterion in restricting or regulating household chemicals for hygienic reasons.

We have furnished information as to the toxicity parameters of household chemicals, the methodological approaches to arriving at the threshold dozes of exposure to household chemicals involving the toxicological and other indicators of the organism. Synthetic detergents have been used as an example to evaluate the allergenic, mutagenic, carcinogenic and teratogenic effect of household chemicals. Toxicity has been discussed as the basic criterion for restricting certain household chemicals of hygienic reasons.

PREDICTION OF THE TOXICITY OF SUBSTANCES

N. A. Egorova

Our investigations have made it possible to ascertain the mathematical dependence between the indices of chronic toxicity (maximum non-effective dose (MND) and acute toxicity (DL_{50}) and the chemical structure of some groups of substances: derivatives of benzene, phenol, phenyl urea, aniline ethers of fatty acids, aldehydes, ketones, amino compounds of the fatty series. The initial data on toxicometric parameters have been taken from Soviet works on hygienic standardization of substances in water, and only those compounds were chosen for investigation for which the chronic test MND values had already been established. The following parameters were used to characterize the structural peculiarities of substances: octanol water partition coefficient (P), Hansch's hydrophobity constant (π), molecular refraction (mR), Hammett's electron constant (σ), electron constant for aliphatic compounds (σ_1), Taft's steric constant (E_s) /Handsch et al., 1973; Jaffe, 1953; Taft, 1956).

The initial data were analyzed on a computer, coefficients of binary and multiple correlation between the toxicity indices and the physico-chemical constants were calculated for each group of substances with a similar chemical structure. It was also determined whether the dependence of toxicity parameters on the hydrophobic properties of substances (P, π) is of a parabolic nature. The corresponding regression equations were obtained. The best equation for each group of substances was chosen on the strength of two criteria: the highest correlation coefficient (R) and the lowest standard error of determination (S). Indicator coefficients (I) sere introduced into the equations characterizing the contribution of individual substituent groups to the overall activity of the molecule of a certain chemical compound.

In studying the dependences of chronic toxicity indices on physico-chemical constants, associated with the molecular structure of substances, the following results have been obtained.

For benzene derivatives:

$$\lg MND = 0.230\,(\lg P)^2 - 2.180\,\lg P + 0.840\,J_I + 1.044\,J_2 + 2.063$$

$$n = 18 \qquad K = 0.893 \qquad S = 0.505$$

where J_I is the indicator coefficient characterizing the CH_3 group contribution to the overall activity of chlorine- and nitro derivatives of benzene, J_2 is the indicator coefficient characterizing the contribution of hydrocarbon substituents to the activity of benzene derivative molecules which do not contain chlorine- or nitrogroups.

For phenol derivatives the following equation proved to be the most suitable:

$$\lg MND = 0.176\,\lg P + 0.466\sum\sigma - I.967\,J_{NO_2} - 2.907\,J_{CH_3} -$$
$$- I.225\,J_{CI} - I.153\,J_{ortho} - 0.530$$

$$n = 23 \qquad R = 0.909 \qquad S = 0.577$$

where NO_2, CH_3, CL are the indicator coefficients for substituent groups in the phenol molecule, J_{ortho} is the indicator coefficient for substituents in ortho-position.

In the group of aldehydes, ketones, and ethers of fatty acids the interrelation between the chemical structure and chronic toxicity was expressed by the following equation:

$$\lg MND = -I.242\sum\pi^2 + 4.234\sum\pi - 0.080\sum\sigma - 2.048\,J_1 -$$
$$- I.816\,J_2 - 2.949$$

$$n = 12 \qquad R = 0.952 \qquad S = 0.391$$

where J_1 is the indicator coefficient for compounds having double bonds in the molecule, J_2 is the indicator coefficient for methyl ethers of fatty acids, aldehydes, and ketones containing a benzene ring in the molecule.

For phenyl urea derivatives the best equation was lg MND = $- 0.097\sum\pi - 0.590\sum\sigma + 0.173\sum\sigma_I + 0.132E_s - 0.888J_1 + 0.232$

$$n = 10 \qquad R = 0.854 \qquad S = 0.37I$$

where J_1 is the indicator coefficient for substances having CH_3O and HO groups.

MND dependence on the chemical structure of amino compounds of the fatty series was expressed by the following parabolic equation:

$$\lg MND = -0.030\,(\lg P)^2 + 0.6II \lg P - 0.725\sum\sigma_1 + 0.709 \sum E_s - 0.724\,J_1 - I.726$$

$$n = 14 \qquad R = 0.876 \qquad S = 0.429$$

where J_1 is the indicator coefficient for disubstituted and isocompounds.

For aniline derivatives the following equation was calculated:

$$\lg MND = 2.974 \lg P - 2.070\sum\sigma - 0.234\sum mR + 0.962 \sum E_s - 3.I4I\,J_1 - 5.I22$$

$$n = II \qquad R = 0.973 \qquad S = 0.373$$

where J_1 i the indicator coefficient for aniline CH_3 - derivatives.

It proved impossible to ascertain the interrelation between the MND of aliphatic and cyclic hydrocarbons and their chemical structure, evidently because of the insufficient number of substances taken for analysis.

The obtained equations expressing the dependence of MND on the physico-chemical constants had the following statistical parameters: correlation coefficients 0.854–0.973, mean ratios between theoretical and experimental values 2.3–3.8 and only for one out of the 98 substances the MND theoretical / MND experimental ratio was equal to 12.

To increase the information content of the mathematical model used in our investigations the combined Hansch - Free - Wilson method was used, which made it possible to calculate the toxicity parameters of substances with a higher accuracy than that of Hansch's classical method.

It should be noted that even for the same group of chemical compounds the equations characterizing chronic and acute toxicity are different. This may be explained by the action mechanism of a substance for a single administration differing from that for a chronic intake by the organism. The possibility of considerable differences in the course of acute and chronic intoxications was pointed out by N.A. Lazarev as far back as 1938. That is why at the present stage of inquiring into the "structure - activity" problem it should be regarded as justified to elaborate the calculation methods only as applied to individual groups of chemical compounds with a similar structure.

THE RESULTS OF ACUTE EXPERIMENTS USED TO PREDICT THE CHRONIC TOXICITY OF SUBSTANCES

In the development of the theory and practice of predicting the acute effect of substances resulting from their prolonged intake by the organism in small doses, investigators have repeatedly resorted to acute experiments on animals.

Indeed, a single administration of substances in large doses lethal for animals does not take much time and resources but gives one a sufficiently clear idea of the nature and intensity of the substance's toxic action. The median lethal doses, DL_{50}, obtained from such experiments, serve as reliable toxicometric parameters that can easily be used in calculations for a tentative assessment of chronic toxicity levels for different substances. Several attempts have been made at ascertaining the mathematical dependences between the maximum non-effective doses (MND) of a chronic test, or directly the MPC, according to the toxicological indication of harmfulness, and the DL_{50} values for substances studied by specialists in the field of water hygiene /S.D. Zaugol'nikov et al., 1978; G.N. Krasovsky et al., 1979/. We, in particular, previously proposed the following equation to calculate MND from DL_{50}:

$$\lg MND = 0.88 \lg DL_{50} - 3.54$$

$$n = 260 \qquad r = 0.529 \qquad s = 1.061$$

The results proved to be both reassuring, since they indicated the existence of a correlation between the acute and chronic toxicity indices of substances, and disappointing, since the ascertained correlation proved to be poorly pronounced, and the equations derived from it produced a considerable error and did not allow a reliable determination of the MND value. The insufficient accuracy of equations used to calculate MND from DL_{50} may be due to the fact that median lethal doses take care of only one aspect of the substance's action - its toxicity, while chronic action includes not only toxicity but also the cumulative action of chemical compounds. Hence, the unsatisfactory accuracy and practical inapplicability of such equations in calculating MND for high-molecular compounds. To ensure greater accuracy provided by equations it is necessary to introduce a component accounting for the cumulative action of substances. Information on the degree of a substance's cumulative action can be obtained from the acute test itself. For instance, B.M. Shtabsky /1974/ proposed to use to this end the median lethal time of animals in an acute test. The prerequisites for using a time parameter to assess cumulative properties are provided by the observations made by experimenters-toxicologists over many years: as a rule, the later animals die after the administration of lethal doses of a substance, the more pronounced are its cumulative properties. For example, after a single administration of highly cumulative mercury in doses close to DL_{50} animals die 7-10 days later, i.e. after the interval necessary for a specific lesion of renal tissue, the so-called "corrosive sublimate of the kidney". Under the effect of lethal doses of weakly cumulative organophosphorus compounds, e.g., methylacetophos, the animals die within the first day of intoxication. It remained unclear, however, what the best way to characterize the time parameter was and how to calculate the median lethal time for animals in an acute test. The classical method of determining the median lethal time of animals using probit-analysis /M.L. Belen'ky, 1963/ gives the value of the median lethal time only for one of the administered doses close to DL_{50}. In this case the information carried by the acute test is not completely utilized as no account is taken of the variations of the time parameter, caused by the individual sensitivity of animals to the substance in question.

This caused the need for our own method to be elaborated for determining the median lethal time of animals, which was done as follows. As the starting point the table of frequency of animal deaths in an acute test by days and hours of observation was taken. From its data we calculated the median lethal time for each administered dose, taking into account the variations in the lethal times associated with the individual sensitivity of animals or their resistance to the substance studied. The calculated median lethal time values for each of the administered doses of a substance are plotted in a double logarithmic scale and then approximated by a straight line. From the point on the straight line, corresponding to DL_{50}, a perpendicular is dropped onto the X-axis, and the value of TL_{50} - the median lethal time resulting from the median lethal dose is determined. For example, the results of an acute test on white rats with 2,3,6-trichlorotoluene are as follows (Table 1). The median lethal time of animals for each of the administered doses is calculated by multiplying the number of animals by the corresponding lethal time, followed by summing up the obtained values and dividing the sum by the number of animals that died from the given dose of a substance. The TL values and the doses tested in the experiment are then plotted (Fig. 1) and approximated with a straight line. From the point on the straight line, corresponding to DL_{50}, a perpendicular is dropped onto the X-axis. The point obtained is the sought TL_{50} equal to 56 hours.

The method recommended makes it possible to determine TL_{50} with the fullest possible utilization of the acute test data. The TL_{50} value is an integral index and takes into account

Table 1

Data of an acute test on white rats with 2,3,6-trichlorotoluene

Doses, mg/kg	Lethal time, hours						Median lethal time for each dose TL_{50}
	24	48	72	96	120	144	
	number of dead animals						
6000	5	1					(24x5 + 48x1) : 6 = 28
5500	2	2					(24x2 + 48x2) : 4 = 36
5000	1	1	1				(24 + 48 + 72) : 3 = 48
4500			1	1			(72 + 96) : 2 = 84
4000				1	1		(96 + 120) : 2 = 108
3000						1	144 : 1 = 144

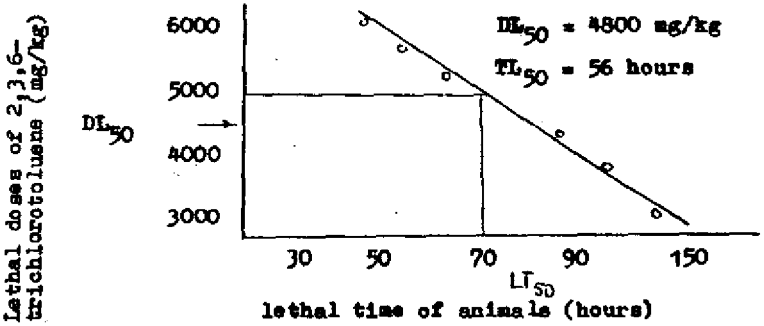


Fig. 1. Determination of TL_{50} from the lethal doses vs. animals' lethal times plot

the time parameter variations associated with animals' individual (higher or lower) sensitivity to the action of a substance administered in doses lower or higher than the median lethal dose.

A method of the quantitative determination of TL_{50} can be used for evaluating the informative significance of this parameter as the one characterizing the cumulative properties of a substance. For this purpose 34 substances have been selected in accordance with the following criteria: (1) availability of the MND of a chronic test for white rats; (2) availability of the DL_{50} for white rats; (3) lethal time of animals in an acute test, registered precisely by days or hours. The median lethal time of animals, TL_{50}, was determined using the elaborated graphical method of calculation. The data were analyzed on an "ES-1033" computer. The correlations between MND, the DL_{50}/MND ratio, proposed as a parameter characterizing the cumulative properties of a substance /G.N. Krasovsky et al., 1976/, and TL_{50} were evaluated and the corresponding correlation coefficients (R), regression equations, mean errors of regression equations (S) were calculated. The logarithms of MND mg/kg, DL_{50} mg/kg, TL_{50} hours and DL_{50}/MND were used in calculations. Since the first analysis of the initial data showed that some substances (chlorine derivatives, phenols, benzene derivatives) differ from the others in the degree of their cumulative properties manifestation (the DL_{50}/MND ratio), indicator coefficients were introduced into the equations, equal to 1 for the above chemical compounds and to 0 for all the other substances.

As a result of the investigations the following regression equation has been numerically solved:

$$\lg DL_{50}/MND = 1.935 \lg TL_{50} + 0.615 J_1 - 1.203 J_2 - 1.388 J_3 + 1.608$$

$$n = 34 \qquad R = 0.882 \qquad S = 0.472$$

where J_{1-3} are the indicator coefficients for the following compounds:

J_1 - aliphatic hydrocarbons with 2 or more chlorine atoms in the molecule;

J_2 - phenols;

J_3 - nitro- and hydroperoxide compounds of benzene;

n is the number of substances.

A high correlation coefficient of equation 1 indicates that there is a clear-cut interrelation between the degree of the cumulative action of substances and the values of animal's median lethal times. The mean ratio between the theoretical and experimental values is 3; only for one substance, methachloroisocyanate, it is 11.

To predict the chronic toxicity of substances from the results of acute tests the following equation was derived:

$$\lg MND = -1.938 \lg LT_{50} + 1.074 \lg DL_{50} - 0.566 J_1 + 1.198 J_2 + 1.383 J_3 - 1.901$$

$$n = 34 \qquad R = 0.925 \qquad S = 0.465$$

where J_{1-3} are indicator coefficients similar to J_{1-3} in equation 1.

The mean ratio between theoretical and experimental values of MND determined by Eq. 2 is 2.9; only for a small number of substances it ranges between 4 and 6. For metachloroisocyanate the ratio is equal to 10.7, which may be due to the fact that structural specific features were ignored when the equations were derived, because there were no compounds of a similar chemical structure among the substances taken for the analysis.

Simultaneous use of DL_{50} (taking care of the first component of chromic effect - toxicity) and LT_{50}, characterizing the cumulative action of substances, i.e. the second component of chronic effect, permits the MND value to be calculated with sufficient accuracy. In this case indicator coefficients are very useful as they help include the specific features of the cumulative effect of some chemical compounds in the equation.

The equations for predicting MND of a chronic test from DL_{50} and LT_{50} values, as well as DL_{50}/MND ratios with respect to LT_{50} can be recommended to be used for hygienic standardization of substances in water. They are obtained in a short-duration and not too laborious acute experiment yielding an accurate and reliable toxicometric parameter LT_{50}. The accuracy of determining the median lethal time of animals depends entirely on how thoroughly the times of animal deaths in the experiment are registered by the experimenter. LT_{50} is easy to calculate and the information derived from this parameter is quite valuable since determination of LT_{50} seems to be the simplest and rather an accurate method for assessing the cumulative action of substances.

Regrettably, in recent years researchers have not given the time parameter in an acute experiment the attention it deserves. This makes it difficult and even impossible to use the results obtained for predicting the cumulative and chronic toxicity of substances.

REFERENCES

1. Belen'ky M.L. Elements of quantitative assessment of the pharmacological effect. 2nd ed., rev. and enl. - Leningrad, Medgiz, Leningradskoye otdeleniye, 1963, pp. 152 (in Russian).
2. Krasovsky G.H., Vasyukovich L.Ya., Varshavskaya S.P., Borisov A.I., Khitrova N.I., Chariyev O.G., Shortanbayeva M.A. Approaches to substantiating the classification of chemical pollutants in water. In: "The hygienic aspects of environmental protection", iss. 4, Moscow, 1975, pp. 26-30 (in Russian).
3. Shtabsky B.M. A rapid method for the hygienic standardization of harmful substances. - Gigiyena truda i profzabolevaniya, 1974, No. 1, pp. 23-28 (in Russian).
4. Hammet L.P. Physical organic chemistry. London, 1970, p. 356.
5. Hansch C., Fukunaga J. Designing biologically active materials. - Chem. Technol. 1977, 7, pp. 120-128.
6. Jaffe H.H. A reexamination of the Hammet equation. - Chem. Reviews, 1953, v. 53, pp. 191-261.
7. Leo A., Hansch C., Elkina P. Partition coefficients and their uses. - Chem. Rews, 1971, 71, pp. 525-616.
8. Taft R.W. Separation of polar, steric and resonance effects in reactivity. - In: Steric effects in organic chemistry. New York, 1956, pp. 556-675.

CALCULATION METHODS FOR REGULATING CHEMICAL ATMSOPHERIC AIR POLLUTANTS

L. A. Tepikina

1. Introduction

In view of the steadily extending range of chemicals used in industry, agriculture, and at home, it is becoming important to speed up the evaluation of their toxicity and the establishment of tentative safe exposure levels. This has to be done in order to obviate the disproportion between the increasing number of new chemicals applied in industry and the real possibilities of studying and hygienically rating them. One of the most promising ways to resolve the problem is to develop a mathematical method that permits prediction of the safe concentration of air-borne pollutants on the basis of short-term experiments and the MACs established for other environments (air of working zone, inland waters) as well as from the physico-chemical properties of the chemicals.

The theoretical principles of applying calculation methods for predicting the toxicity of substances from their physico-chemical properties have been set forth by the prominent Soviet toxicologist N.V. Lazarev [1].

In later years, Leningrad toxicologists have been systematically trying to elucidate the relationship between the indicators of biological activity of substances and their physico-chemical properties [2, 3].

At present, a wealth of data are available concerning the calculation-based rating of harmful substances in working zone air [2,3,4,5,6,7,8,9], atmospheric air, and inland waters [10,11,12,13].

Most of the calculation methods rely upon a common principle, namely, finding correlations between the established values specified in hygienic standards and various physico-chemical and biological parameters. The calculation methods of rating quintessentialize years of practical experience in hygienic standardization. Naturally, calculation methods are not an adequate substitute for experimental substantiation of MACs, especially as regards substances exhibiting specific and remote effects (allergenic, embryological, mutagenic, etc.).

Thus, the calculation methods for establishing hygienic rates may be classified as follows:

(1) establishment of safe exposure levels based on toxicometric parameters and found in short-term experiments;

(2) rating based on the MACs established for other environmental conditions;

(3) rating based on the physico-chemical characteristics of chemicals.

2. Methods of Finding Appropriate Formulas for Calculating Certain Toxicometric Parameters of Harmful Substances

The currently existing methods of calculating the TSEL of harmful substances are based on a correlation between their toxicity parameters, noneffective concentrations (MAC), and physico-chemical properties. Here, a logarithmic form of correlation between the resultant and factorial indicators, such as

$$\log y = a_0 + a_1 \log x$$

or

$$\log y = a_0 + \sum_{i=1}^{n} a_i \log x_i$$

is primarily used in the case of a multiple correlation, which, according to some researchers, is reasonable in view of "the logarithmic dependence of the effect of poisons on their dosages or concentrations".

Another reason why the use of logarithmic correlation formulas has been successful may be the usual consequence of "rectification" of any curve representing the nonlinear relation between resultant and factorial indicators in the logarithmic space.

In this case, the correlation coefficient (R) will increase as the relationship of interest approaches a power function, often reaching high value. However, since no studies have been conducted, to the best of our knowledge, with a view to find an optimal correlation, it is still questionable whether the logarithmic form is the best for a given pair of indicators. In the literature, one can find some instances where other correlation formulas are used, although nothing is said about their advantages over the alternatives. For example, Yu.S. Kagan recommends the following formula for pesticides:

$$y = a_0 + a_1x,$$

which is essentially a linear regression equation.

This is to say that taking the logarithm of the parameters to derive the desired form of correlation is not a universal solution and that each individual case requires proof that the formula chosen for calculating the TSEL is the best among the examined ones. Therefore, our work [14] has involved, primarily, development of a method for selecting the best formula and the algorithm for handling the numerous routine operations inevitable in this process.

While determining the appropriate form of correlation between sequences of empirical data (in our case this role will be performed by given values of toxicometric indicators of the substances), the following equations are usually considered in view of their use: straight line; exponential, power and semilogarithmic function, hyperbola, parabola, etc. To standardize the process of determining the coefficients of the equations the initial data are transformed in such a way that each particular equation acquires a form of a linear regression model [15,16,17]. In this case, we somehow enlarge the list of formulas (to ten) due to the transformation applicable to all sequences of data considered herein (Table 1).

Selection of the best form of correlation among the examined ones is far from being simple due to certain peculiarities of the initial data which essentially affect the validity of the dispersion estimates the most important of which are the following: inhomogeneous distribution of the indicator values within the area under examination (stratification), ambiguity among the values of the indicator taken as a dependent variable (resultant) with respect to the definite value of the independent variable (factorial), etc. [18]. The traditional method of "deleting" suitable values of toxicometric indicators and MACs of the substances from the initial list of data was found to be incorrect, for such an approach cannot be considered objective, even though the selection criteria were previously formulated, and, therefore, it can lead, in principle, to the establishment of selection of any correlation given a priori. For this reason, according to the method recommended herein, the criterion for selection is based on the comparison

Table 1. Types of Correlation Formulas

Elementary function	Reduced (rectified) form of elementary function
1. Straight line	$y = \beta_o + \beta_1 x$
$y = a_o + a_1 x$	$a_o = \beta_o \quad a_1 = \beta_1$
2. Exponential function	$\log y = \beta_o + \beta_1 x$
$y = a_o + a_1^x$	$\log a_o = \beta_o \quad \log a_1 = \beta_1$
3. Semilogarithmic function	$y = \beta_o + \beta_1 \log x$
$y = a_o + a_1 \log x$	$a_o = \beta_o \quad a_1 = \beta_1$
4. Power function	$\log y = \beta_o + \beta_1 \log x$
$y = a_o x^{a1}$	$\log a_o = \beta_o \quad a_1 = \beta_1$
5. Parabola	$y = \beta_{o_2} + \beta_1 x$
$y = a_o + a_1 x + a_2 x^2$	$a_o = \beta_o \quad a_1 = 2\beta_o\beta_1 \quad a_2 = \beta_1^2$
6. and its	$y = \beta_o + \beta_1 \sqrt{x}$
$y = a_o + a_1 \sqrt{x}$	$a_o = \beta_o \quad a_1 = \beta_1$
7. varieties	$\sqrt{y} = \beta_{o2} + \beta_1 \sqrt{x}$
$y = a_o + a_1 \quad x + a_2 x$	$a_o = \beta_o \quad a_1 = 2\beta_o\beta_1 \quad a_2 = \beta_1^2$
8. Hyperbola	$\frac{1}{y} = \beta_o + \beta_1 x$
$y = \frac{1}{a_o + a_1 x}$	$a_o = \beta_o \quad a_1 = \beta_1$
9. and its	$y = \beta_o + \beta_1 \frac{1}{x}$
$y = a_o + a_1 \frac{1}{x}$	$a_o = \beta_o \quad a_1 = \beta_1$
10. varieties	$\frac{1}{y} = \beta_o + \beta_1 \frac{1}{x}$
$y = \frac{x}{a_o + a_1 x}$	$a_o = \beta_o \quad a_1 = \beta_1$

of the total number of validity evaluations of the formulas given in Table 1, that is, the estimation of the most resultant (as regards the standard deviation criterion, SD_{min} - root-mean-square deviation of calculated indicators from the initial ones in the normal, untransformed space) and the most reliable (using Fisher's F - criterion) mathematical model. As additional evaluation, one can consider the correlation coefficient (R and its estimation from Student's T_R) and the error involved in determination of the regression coefficient (Δ b). As a rule, these estimates undergo simultaneous changes. In other words, the maximum correlation corresponds to the best estimates. However, certain distortion of the correlation estimate is observed in a number of cases. Thus, for example, the maximum correlation corresponds to such a form of correlation which does not have the maximum estimates with respect to SD- and F-criteria. This can be attributed to both the above-described peculiarities of the initial data and the effect of the calculation scheme, namely: calculation of the formula coefficients is based on attainment of the SD_{min} - criterion to transform the calculated data from the experimental, initial ones, while the validity of the mathematical model thus obtained is evaluated by comparing the initial and calculated values of the indicators. In this case, the model using the SD_{min}- criterion should be preferably selected, for we primarily are interested in attaining the least deviation of the calculated data from the initial ones. In more complicated cases of deviation, which at the same time are less frequent, a non-formal selection based on the same practical principle is also possible.

In view of the above, the following procedure for selecting the empirical formula can be stated:

1. For each type of transformation, calculate the coefficients a and b of the formulas, determine correlation coefficients R, the value of Student's T_R - criterion for estimation of R, Δb - evaluation of the error involved in determination of the coefficient Δb.

2. Determine the calculated values of the resultant indicators according to each formula.

3. Determine the the values of SD and Fisher's F-criterion according to the calculated and initial resultant data.

4. Make sure that the optimal formula has been selected with reference to the minimum SD in the sequence obtained.

As a rule, numerous calculations required by this method exclude any manual operations. Therefore, a special programme using Fortran language was elaborated to provide the necessary data for speedy and efficient selection of the formula which can be the best among the listed ones. If necessary, the list of formulas given in Table 1 can be expanded in case of appropriate modification of the programme. There is no need to absolutize any data found with the aid of the above-described method. These data can be correlated if the initial parameters are added. The programme can be repeatedly applied for efficient examination.

The method and the programme were used for determining the correlation between certain toxicometric parameters and MACs in various environments as well as for establishing the calculation formulas for the TSEL of atmospheric air pollutants on the basis of MAC_{wz} depending on the hazard class of the substance (Table 2).

Table 2. Results of Establishing a Correlation Between MAC_{ad} (average daily) and MAC_{wz} (in the air of the working zone) for Substances of Hazard Class 2 ($n = 56$)

Correlation type		Formula type	Coefficients		R	T_R	SD	F	
y	x		a	b					
y -	x	1	-0.035	0.0603	0.723	7.68	0.211	59.1	$p < 0.001$
log y -	x	2	-1.990	0.1000	0.508	4.33	0.204	29.1	$p < 0.001$
y-	log x	3	0.114	0.215	0.426	3.46	0.276	12.0	$p < 0.01$
log y-	log x	4	-1.730	0.456	0.380	3.04	0.308	3.22	$p < 0.1$
$\sqrt{y}$ -	x	5	0.087	0.045	0.677	6.76	0.201	29.8	$p < 0.001$
y -	$\sqrt{x}$	6	-0.132	0.197	0.590	5.37	0.246	28.9	$p < 0.001$
$\sqrt{y}$ -	$\sqrt{x}$	7	0.015	0.155	0.589	5.36	0.250	8.37	$p < 0.001$

Table 2 shows that with respect to the total amount of estimates the priority should be given to formulas 5,2,1; the logarithic form of correlation was found to be less precise as regards the SD criterion.

The results of the search for the calculation formulas of TSEL have convincingly shown that at the present level of our knowledge concerning the toxicity of chemicals we cannot consider one or another form of correlation between such and such toxicometric indicators to be optimal. This means that in each specific case we should select such a formula which can be considered the best approximation to the unknown correlation between the indicators under examination.

3. Methods of Establishing Tentative Safe Exposure Levels of Atmospheric Air Pollutants

The tentative safe exposure level (TSEL) is a provisional hygienic state standard specifying the maximum allowable concentrations of a pollutant in atmospheric air.

The TSEL is a parameter used in preventive sanitary inspection for timely identification of the requirements to the health protecting procedures to be carried out as well as for determining maximum allowable emissions (MAE) into the atmosphere by industrial enterprises.

The TSEL are determined by calculations based upon: toxicometric parameters of substances and MACs in other environments; physico-chemical constants.

However, if no toxicity data are available, the TSEL cannot be recommended after calculations based only on the physico-chemical parameters of a substance. In this case, reference should be made to the toxicity of compounds with similar physico-chemical and biological properties.

The TSEL cannot be established for substances exhibiting a potential hazard of remote effects (carcinogenic, mutagenic, embryo- and ganodotoxic, etc.) if the toxicometric parameters and MACs in other environments have been defined without account for these effects.

3.1. Prediction of TSEL from Toxicometric Parameters and MACs in Other Environments

Equations have been derived for rating pollutants in atmospheric air, based on a correlation between the short-time MAC (MAC_{st}), average daily MAC (MAC_{ad}), and some parameters of reflex and toxic effects of substances. Yu.A. Krotov [22] has established a correlation between MAC and olfactory threshold or threshold of action on the bioelectric activity of the brain:

$$\log \text{MAC}_{st} = 0.96 \log x_1 - 0.51 \qquad (3.1)$$

where x_1 is the olfactory threshold (mg/m^3);

$$\log \text{MAC}_{st} = 0.93 \log x_2 - 0.45, \qquad (3.2)$$

where x_2 is the threshold of visual sensation (mg/m^3);

$$\log \text{MAC}_{st} = 0.97 \log x_3 - 0.23, \qquad (3.3)$$

where x_3 is the threshold of bioelectric activity of the brain.

Yu.A. Krotov [22] has also proposed a formula for calculating the average daily MAC from average lethal concentrations (LC_{50} in mg/liter):

$$\log \text{MAC}_{ad} = 0.58 \log LC_{50} - 1.6 \qquad (3.4)$$

at $n = 59$, $R = 0.68$, and $S_{xy} = 0.68$.

M.M. Kochanov and co-workers [2[illegible]] have established a rather close correlation between MAC_{ad} and average lethal doses (LD_{50} with ingestion of g/kg of the substance) and concentrations (LC_{50}, mg/liter):

$$\log \text{MAC}_{ad} = -0.7 + 1.7 \log LC_{50} - 0.8 \log LD_{50} \qquad (3.5)$$

Most of the calculation formulas have been derived through the establishment of correlations between MACs in atmospheric air and in the air of the working zone$_{wz}$.

Table 3.1. Calculations Formulas and their Statistical Estimates

Source, year	Formula	n	R
Ye.I.Spynu et al. [24], 1969	$\log MAC_{ad} = -2.16+0.88 \log MAC_{wz}$	30	0.69 (3.6)
A.O.Loyt et al., [25], 1971	$\log MAC_{ad} = -2.0+0.86 \log MAC_{wz}$	40	0.65 (3.7)
Yu.A.Krotov [22], 1975	$\log MAC_{ad} = -1.77+0.62 \log MAC_{wz}$	75	0.70 (3.8)
V.G.Ashkenazy et al., [26], 1977	$\log MAC_{ad} = -1.74+0.53 \log MAC_{wz}$	89	0.61 (3.9)

It can be seen that the formulas are closely similar and the coefficients of the equations differ within the error of their determination.

We [27] have also established a correlation and derived correlation formulas for MACs in various environments. In particular, the following formulas can be recommended for atmospheric air:

$$TSEL_{atm}\ (mg/m^3) - (0.110 - 0.0654 \sqrt{MAC_{wz}})^2 \qquad (3.10)$$

at $n = 117$, $R = 0.78$, $SD = 2.31$, $F = 76.1$, and $p < 0.001$.

$$TSEL_{atm}\ (mg/m^3) - 0.0351 - 0.827\ MAC_{water} \qquad (3.11)$$

at $n = 81$, $R = 0.71$, $SD = 1.16$, $F = 81.3$, and $p < 0.0001$.

Analysis of the general correlation between MAC_{atm} and MAC_{wz} reveals a striking difference between the extreme numbers in the series, reaching several orders of magnitude. For example, MAC_{wz} of dichlorofluoromethane, hazard class 4, is 3000 mg/m^3, while MAC_{ad} of benzopyrene, hazard class 1, is 0.1 µg/100 m^3. Therefore, since any mathematical formula (formulas 3.1 and 3.10–3.11) permits calculating the average data in a series, the TSEL calculated using all the above formulas may be overestimated for substances of hazard class 1 and underestimated for those of hazard class 4.

The following formulas may be recommended for calculating the TSEL of pollutants in atmospheric air [14] :

Hazard class 1

$$\log TSEL_{atm} = -0.641 + 1.35 \log MAC_{wz} \qquad (3.12)$$

at $n = 14$, $R = 0.91$, $SD = 0.01$, $F = 9.2$, and $p < 0.05$.

Hazard class 2

$$TSEL_{atm} = (0.097 + 0.0445\ MAC_{wz})^2 \qquad (3.13)$$

at $n = 56$, $R = 0.68$, $SD = 0.201$, $F = 29.8$, and $p < 0.001$,

or $$\log TSEL_{atm} = -1.99 + 0.1\ MAC_{wz} \qquad (3.14)$$

at $n = 56$. In this formula, at the same SD and at $F = 29.1$, the correlation factor is lower ($R = 0.51$).

Hazard class 3

Here, the correlation between the parameters of interest was found to be below average ($R = 0.39$) with statistical estimates of low reliability because of data stratification. For this reason, the formula cannot be recommended.

Hazard class 4

$$TSEL_{atm} = (0.112 + 0.0649\sqrt{MAC_{wz}})^2 \qquad (3.15)$$

at $n = 21$, $R = 0.71$, $SD = 5.66$, $F = 17.3$, and $p < 0.01$.

It is known that the most exact reliable equations are those derived for groups of chemical compounds with similar physico-chemical properties and biological activity. We [27,28] have derived formulas for some groups of chemical compounds as well.

For aldehydes and ketones:

$$TSEL_{atm} = 0.0189 + 0.00165\ MAC_{wr} \qquad (3.16)$$

at $n = 8$, $R = 0.96$, $SD = 0.037$, $F = 68.0$, and $p < 0.001$.

$$TSEL_{atm} = -0.078 - 0.000033\ LD_{50} \qquad (3.17)$$

at $n = 7$, $R = 0.89$, $SD = 0.065$, $F = 18.7$, $p < 0.05$, and $LD_{50} > 250$ mg/kg.

$$\log TSEL_{atm} = -2.14 + 0.00015\ LD_{50} \qquad (3.18)$$

at $n = 7$, $R = 0.61$, $SD = 0.075$, $F = 7.48$, $p < 0.05$, and $LD_{50} > 250$ mg/kg.

$$\log TSEL_{atm} = -2.34 + 0.0000132\ LC_{50}\ (mg/m^3) \qquad (3.19)$$

at $n = 7$, $R = 0.92$, $SD = 0.04$, $F = 28.7$, and $p < 0.05$.

For aromatic hydrocarbons of the benzene series:

$$\log TSEL_{atm} = -1.88 + 0.22\ LC_{50}\ (mg/liter) \qquad (3.20)$$

at $n = 17$, $R = 0.6$, $SD = 0.144$, $F = 2.32$, and $p < 0.05$.

$$\log TSEL_{atm} = -1.74 + 0.625 \log LD_{50}\ (g/kg) \qquad (3.21)$$

at $n = 24$, $R = 0.6$, $SD = 0.124$, $F = 2.31$, and $p < 0.05$.

$$TSEL_{atm} = (0.122 + 0.00588\ MAC_{wz})^2 \qquad (3.22)$$

at $n = 26$, $R = 0.66$, $SD = 0.098$, $F = 8.98$, and $p < 0.001$.

For metals:

$$TSEL_{atm} = -0.00036 + 0.0000159\ LD_{50}\ (mg/kg) \qquad (3.23)$$

at $n = 11$, $R = 0.79$, $SD = 0.01$, $F = 14.5$, and $p < 0.05$.

$$TSEL_{atm} = 0.00104 + 0.00327\ MNED\ (mg/kg) \qquad (3.24)$$

at $n = 11$, $R = 0.99$, $SD = 0.0025$, $F = 337$, and $p < 0.001$.

For inorganic vapours, gases, and aerosols:

$$TSEL_{atm} = (0.162 + 0.127\sqrt{LC_{50}\ (mg/liter)})^2 \qquad (3.25)$$

at $n = 12$, $R = 0.6$, $SD = 0.4$, $F = 3.59$, and $p < 0.05$.

$$TSEL_{atm} = (0.07 + 0.017\ Lim_{cm})^2 \qquad (3.26)$$

at $n = 12$, $R = 0.7$, $SD = 0.368$, $F = 4.91$, and $p < 0.05$.

$$TSEL_{atm} = (0.112 + 0.0268\ MAC_{wz})^2 \qquad (3.27)$$

at $n = 19$, $R = 0.7$, $SD = 0.27$, $F = 5.83$, and $p < 0.05$.

For organophosphorus pesticides:

$$\log TSEL_{atm} = -1.79 + 0.693 \log MAC_{wz} \qquad (3.28)$$

at $n = 8$, $R = 0.54$, $SD = 0.006$, $F = 2.58$, and $p < 0.05$.

$$TSEL_{atm} = 0.00249 + 0.0125\sqrt{MNED} \qquad (3.29)$$

at $n = 9$, $R = 0.77$, $SD = 0.003$, $F = 10.5$, and $p < 0.05$.

3.2. Calculation of TSEL Based on Physico-Chemical Properties

For predicting the TSEL of atmospheric air pollutants, simple physico-chemical constants (boiling point, molecular weight, density, vapour pressure, etc.) are used.

Proceeding from analysis of the correlation between short-time MACs of 25 benzene derivatives and their molecular weight, M.G. Andreyeshcheva [20] has recommended a formula for calculating the $TSEL_{st}$ of organic substances with molecular weights ranging from 32 to 330:

$$\log y = -8 \log x + 14.75 \qquad (3.30)$$

at $n = 25$, $R = 0.937$, and $S_{xy} = 0.024$, where $\log y$ is the

$TSEL_{at}$ in mg/m^3 of the organic substance, and x is the molecular weight (MW). The following coefficients (K) must be used in the calculations:

K = 1.0 for MW from 147.0 to 199.9,

K = +2.0 for MW from 200.0 to 264.9,

K = +3.0 for MW from 265 and above (up to 330),

K = -1.0 for MW from 70.0 to 44.9,

K = -3.0 for MW from 45.0 to 32.0.

N.G. Andreyeshcheva has also proposed a formula for calculating the TSEL, from the boiling point (b.p.), of substances with boiling points ranging from 20 to 315°C:

$$\log y = -5.6 \log x + 11.2 \qquad (3.31)$$

at $n = 25$, $R = 0.978$, and $S_{xy} = 0.011$, where log y is the $TSEL_{at}$ of the organic substance (mg/m^3) and x is its b.p. in °C at 760 mm Hg.

The following coefficients are involved in the calculation of log y:

K = +1 at b.p. 270°C,

K = -1 at b.p. from 77°C,

K = -2 at b.p. from 60°C,

K = -3 at b.p. from 48°C,

K = -4 at b.p. from 35°C and below.

N.G. Andreyeshcheva has also recommended formulas for calculating the TSEL of benzene derivatives from the saturated vapour density at 20°C, refraction index, molecular refraction and density.

In recent years, prediction of toxicometric parameters has been based on, along with the usual physico-chemical constants, calculated parameters of the electron structure of molecules (energy levels, atomic charges, bond orders, etc.), as well as the physico-chemical properties closely associated with the chemical structure of molecules (dipole moment—μ; $\sum\sigma$, σ the sum of Hammett's σ -constants; $\sum\alpha$, the sum of nuclear quadrupole resonance (NQR) increments; etc.).

M.L. Krasovitskaya and co-workers [21] have found a close correlation between the above properties of bromobenzene polysubstituents and acute toxicity indicators (average lethal doses at ingestion - LD_{50}) and intraperitoneal administration (LD_{50ip}). The investigators have shown that the predicted parameters differed from the experimental ones by a factor of 1.3-1.5.

This approach can be used for predicting toxicity and hazard of newly synthesized chemicals as well as safe exposure levels with the aid of the known formulas including acute toxicity parameters.

In conclusion, we should like to emphasize again that the equations employed for establishing tentative safe exposure levels must be derived with due account of the biological aspects of the phenomenon under investigation. Therefore, formulas based on the toxicometric parameters and MACs of chemicals should be used in the first place. Equations based on physicochemical properties may serve as a reference in determining the toxicity and hazard of the synthesized compounds.

REFERENCES

1. N.V. Lazarev, Non-Electrolytes: Their Biological and Physicochemical Classification, Leningrad, 1974, 270.
2. A.A. Golubev et al. Quantitative Toxicology, Leningrad, Meditsina, 1973.
3. V.A. Filov and Ye.I. Lyublina, Correlation of the Composition, Structure, and Properties of Chemical Compounds with Toxicity Indicators and Their Use for Prediction Purposes, In: "Fundamentals of General Industrial Toxicology" (manual) edited by N.A. Tolokontsev and V.A. Filov.
4. G.N. Zaeva and N.K. Kulagina. Express Methods of Establishing Maximum Allowable Concentrations. In: "Principles and Methods of Establishing Allowable Concentrations of Harmful Substances in the Air of the Working Zone", Proceeding of the International Symposium of Scientists from Socialist Countries, November 25-29, 1968, Moscow, 1970, 23-24.
5. S.D. Zaugolnikov, M.M. Kochanov et al. Express Methods for Determining the Toxicity and Hazard of Chemicals, Leningrad, Meditsina, 1978, 184.
6. Ye.I. Lyublina and L.V. Rabotnikova. The Possibility of Predicting the Toxicity of Volatile Compounds from Their Physical Constants, Gigiene i sanitariya, 1971, 8, 33-37.
7. Yu.S. Kagan. Differentiated Approach to Establishing Calculated TSEL of Industrial Groups of Pesticides. In: "Application of Mathematical Methods of Estimation in Predicting the Real Hazard of Pesticide Accumulation in the Environment and Living Organisms", Proceedings of the 2nd All-Union Symposium, October 12-14, 1976, Kiev, 1976, 78-81.

8. K.K. Sidorov and A.B. Shapiro, A Method of Calculating the TSEL of Harmful Substances in the Air of the Working Zone, Proceedings of the 2nd All-Union Symposium, October 12-14, 1976, Kiev, 1976, 81-83.

9. N.G. Ivanov. An Express Method of Determining the Safe Exposure Levels of Poisons, Based on Monitoring of Specific Manifestations of Intoxication, Proceedings of the 2nd All-Union Symposium, October, 12-14, 1976, Kiev, 1976, 82-85.

10. A.A. Golubev and V.G. Subbotin. On the possibility of Applying a Calculation Method of Establishing Tentative Safe Exposure Levels of Harmful Substances in Inland Waters. In: "The Hygiene of Application, Toxicology of Pesticides, and Clinical Manifestations of Poisoning", Kiev, 1968, vol. 6, 284-287.

11. G.N. Krasovsky and N.A. Yegorova. Methods of Predicting and Calculating the Sanitary and Toxicological Parameters for the Purposes of Hygiene Standardization. In: "Recent Advances in the Diagnosis, Treatment, and Prevention of Major Diseases and Research Methods", Moscow, 1971, 118-120.

12. G.N. Krasovsky et al. Topical Problems of Municipal Toxicology in Connection with Chemical Pollution of Water Basins. In: "Pharmacology, Chemotherapeutic Drugs, Toxicology. Problems of Toxicology. Advances in Science and Technology", Moscow, VINITI, 1974, 15-82.

13. S.A. Shigan. Calculation Methods in Hygienic Standardization of Chemical Water Pollutants", Gigiena i sanitariya, 1976, 11, 15-20.

14. L.A. Tepikina and B.D. Shcherbakov. Methods of Selecting Formulas to Calculate Tentative Safe Exposure Levels (TSEL)

of Chemicals. In: "Hygienic Aspects of Environmental Control", collected papers, A.N. Sysin Institute of General and Municipal Hygiene, USSR Academy of Medical Sciences, Moscow, 1979, 37-43.

15. Ya.Ya. Vainu. Correlation of Dynamic Series, Moscow, Statistika, 1977, 119.
16. T.C. Lee, G.E. Adams, and W.M. Haynes, Computer-Aided Control of Processes. Simulation and Optimization, Moscow, Sovetskoye Radio, 1972, 312.
17. L.Z. Rumshinsky. Mathematical Processing of Experimental Data, Moscow, Nauka, 1971, 192.
18. I.G. Venetsky and G.S. Kildishev. Fundamentals of the Probability Theory and Mathematical Statistics, Moscow, Statistika, 1968, 360.
19. M.I. Lipkin. Analysis of the Premises and Deductions of the Theory of Correlation and Regression. Learned Papers on Statistics, Moscow, Nauka, 1969, vol. XVI, 5-17.
20. N.G. Andreyeshcheva. Methods of Predicting Tentative Thresholds of Reflex Action and Short-Time Maximum Allowable Concentrations of Organic Substances in Atmospheric Air, Gigiena i Sanitariya, 1977, 12, 58-61.
21. M.L. Krasovitskaya, V.N. Bezdvorny, and N.Ye. Ainbinder. Correlation of Acute Toxicity Parameters of Brombenzene Polysusbstituents with Their Physico-chemical Properties and Electron Structure, Gigiena i Sanitariya, 1979, 12, 19-22.
22. Yu.A. Krotov. Calculation Methods of Determining Airborne MAC. In: "Maximum Allowable Concentrations of Harmful Substances in Air and Water", Leningrad, Khimiya, 1975, 86-191.

23. M.M. Kochanov, A.O. Loyt, S.D. Zaugolnikov, and I.I. Stavchansky, Calculation Method of Determining Tentative MACs of Substances in the Atmospheric Air of Populated Centers, Gigiena i Sanitariya, 1974, 8, 79.

24. Ye.I. Spynu and L.N. Ivanova. Prediction of Maximum Allowable Concentrations (MAC) of Some Airborne Chemicals. Gigiena Truda i Profzabolevaniya, 1969, 7, 16.

25. A.O. Loyt, M.M. Kochanov, and S.D. Zaugolnikov. On the Correlation Between MACs of Some Airborne Chemicals in the Working Zone and Populated Areas, Gigiena Truda i Profzabolevaniya, 1969, 7, 18.

26. V.O. Ashkenazy, I.A. Zaks, and Yu.I. Oborin. Statistical Estimation of Correlations Between the MACs of Gaseous Airborne Pollutants in Populated Areas and the Working Zone of Industrial Enterprises, Gigiena i Sanitariya, 1977, 10, 74-75.

27. G.N. Krasovsky, M.A. Pinigin, L.A. Tepikina, Z.I. Zholdakova, N.A. Yegorova, I.P. Ulanova, K.K. Sidorov, and B.D. Shcherbakov. Calculations Methods for Prediction of Safe Levels of Substances in Various Environments. In: "Hygienic Aspects of Environmental Control", collected papers, A.N. Sysin. Institute of General and Municipal Hygiene, USSR Academy of Medical Sciences, Moscow, 1979, 43-45.

28. L.A. Tepikina. Prediction of the TSEL of Aromatic Hydrocarbons of the Benzene Series and Inorganic Compounds, Based on Known Toxicometric Parameters. In: "Effectiveness of Sanitary Environmental Control Procedures in Industrial Areas", Perm, 1982.

Chapter YI

PREVENTIVE TOXICOLOGY OF ECOSYSTEMS

Edited by O.F.Filenko,
Cand of Sci.(Biol)

ENVIRONMENTAL POLLUTION AND ORGANISMS OF AQUATIC BIOCOMMUNITIES

O.F.Filenko

Ecotoxicology involves a broad range of independent scientific problems. Prominent among them is research concerned with the consequences of water pollution. The effect of toxic pollution on aquatic organisms and water systems is studied by aquatic toxicology [7] with a view to drawing up recommendations for their conservation and/or management.

On the assets side, man can pollute water bodies specially to control noxious hydrobiont species. The liabilities include:

- the immediate threat to human health or well-being posed by direct deterioration of water quality;

- reduced production potential of water bodies;

- downgraded quality of commercial organisms;

- secondary deterioration or water quality as a result of disruption of self-purification systems of water bodies and the natural transport pathways of substances.

Plenty of data illustrating the scope and scale of hydrospheric pollution are cited in the literature. Around 40,000 substances are being used today across the world. Yet, only a few of them are manufactured in large quantities. It is estimated that the annual output of 1500 chemical products is 500 tons, that of 100 products is 5000 tons and of 50 products 1,000,000 tons [11].

Introduction of pollutants originating from rocks and anthropogenic sources is the cause of primary pollution. The major sources of anthropogenic pollution include (in decreasing order of importance) mining, domestic effluents, power industry, chemical, petrochemical and gas industries, metallurgy, etc.

Ecological disturbances linked with anomalous reproduction of some hydrobiont groups cause the built-up of the products of their vital activities and subsequently the secondary pollution of water bodies.

Under the impact of physical and chemical factors and live organisms substances entering a water body are usually subjected to various transformations.

The concentration of a substance in water is expressed in mg/l and μg/l, and in bottom sediments and organisms - in mg/kg and μg/kg. In addition, researchers abroad express concentrations in "parts per million" (ppm) or "parts per billion" (ppb).

Substances may enter a hydrobiont via its respiratory and digestion organs and through bodily covers. The uptake intensity depends on the substance's solubility in water and in fats and on its affinity to the biosubstrate molecules. Upon penetrating the external barriers the substance passes into the blood and tissue fluids and spreads across the tissue. The capability of a substance for deposition in tissues may be quantified by several coefficients. Of these, the coefficient of concentration or accumulation (Kc or Ka) represents the ratio of the substance's quantity contained in the organism or individual tissues to the concentration in water. The distribution coefficient is the ratio of the substance's amount in tissues to its amount (concentration) in blood. Greater deposition of a substance in a particular tissue is controlled by concentration selectivity.

An ecologically important index is the coefficient of biopotentiation - the ratio of the substance's amounts in the predator victium tissues. When the ratio exceeds I the substance is accumulated up the trophic chain. The property is usually a feature of lipophilic substances or those having affinity for some chemical groups of biomolecules. Bio-potentiation is hazardous both to ecosystems and humans consuming contaminated food. The routes for a substance's travel and conversion in water are exemplified with mercuty in Fig.1.

In determining toxic concentrations causing a particular effect on hydrobionts, distinction is made between active concentrations (AC), effective concentrations (EC) or lethal concentrations (LC). The impact level is defined as deviation of an index from that of the control in per cent age terms; as deviation from the initial number of individuals; or from the share of individuals in whom a specific effect is induced. The concentration effect varies over time. Consequently, when indicating concentration values causing a certain effect, it is necessary to specify the period within which the effect manifests itself. For this reason, the concentration causing the death of 50 per cent of organisms within 96 hours, for example, is written as LC_{50} within 96 h or LC_{50}^{96}.

The values commonly used to describe a substance's toxicity are LC_0, LC_{25}, LC_{50}, and LC_{100}.

Of the entire range of toxic agents likely to enter water bodies in effluents, washoffs or atmospheric fallout, special attention should be paid to oil products, heavy metals, pesticides, and polychlorinated biphenyls [1].

The total amount of oil pollution in the world ocean is estimated by various authors at 3.26 to 25 million tons annually [2]. For example, in the Torry Canyon accident alone in 1967 119 thousand tons of oil were spilled off the Cornwall coast.

Oil is a mixture of components which, upon entering water, begings to degrade. The light fractions become airborne while the heavy ones settle down to the bottom covering the ground and sedentary aquatic organisms. The half-life of oil in sea water at 10°C is about 1.5 month, at 18-20°C about 20 days, and at 24-30°C up to seven days [6]. The soluble fractions of oil include components posing serious hazard to water inhabitants, such as 3,4-benzo(a)pyrenes, benzanthracenes, etc. Survival of adult hydrobionts may be affected by a fraction of decimals of mg/l. The number of commercial organisms is severely reduced by oil slicks. The consequences of the Torry Canyon accident could be felt off the Cornwall's coast for more than two years [16].

The application of surface - active agents to fight oil spills is ecologically harmful. The agents merely emulsify oil and increase the water-solubility of its fractions. Their use may prove particularly hazardous in land-locked seas and lakes. Emulsification deters volatilization of oil fractions and slows down detoxification.

High rates of natural water pollution by metals have caused not only ecological disruptions, but also human losses [13]. The primary biological hazard is posed by heavy metals (density over 5 g/cm^3) like mercury, copper, nickel, cobalt, lead, zinc, tin and cadmium. Given proper conditions, light metals, for example, aluminum, may become highly toxic to hydrobionts. Since metals proper cannot be destroyed by biogenic and abiogenic factors, their volatilization (mercury) or burial in the bottom sediments are viewed as a detoxifying process.

The solubility and biological impact of metals are affected by the presence in water of other ions and complex-forming agents. The agents like hymic acids increase metal solubility and their accumulation by hydrobionts.

Higher temperatures and oxygen deficiency, lower pH and water hardness increase metal toxicity. Metal deposition is greatest in the kidneys, liver, bone tissue, spleen, and certain glands. Here, metals combine with the lipoprotein structures of membranes and the sulfhydryl groups of proteins. Certain metals like cadmium may compound with proteins to form so-called metal thioneines, with a molecular weight around 10,000.

Metals impair behavioral reactions, fertility, and physiological functions of hydrobionts. Some organic metal compounds are especially toxic. From the viewpoint of their toxicity for hydrobionts they can be presented in the following sequence: Hg > Cd = Cu > Zn > P > Co Cr > As > Mn = Fe > Sn.

<u>Pesticides</u> make a sizeable contribution to the overall toxic pollution of water bodies. About 1000 chemicals of 10,000 trade marks are currently produced in the world. Environmental

persistence of pesticides and toxicity of their conversion products are the factors taken into consideration in their development and recommendations for use. Organochloric and mercuric compounds show the highest build-up capability via trophic links and environmental persistence. The DDT build-up capability via links of the trophic chain may be illustrated by the data for South Florida /9/. The total DDT contents, i.e. total quantities of DDT, DDD and DDE (in Mg/kg) were 0.02 in water, 7 in periphyton, 8 in macrophytes, 16 in sediments, 23 in crayfish, 352 in alligators, and 16,500 in eggs of predatory birds.

Pesticides interfere with the activity of enzymes, membranous structures and permeability, particularly in CNS cells. A temperature rise generally increases the toxicity of organophosphorus compounds, endrin and toxaphene but reduces the toxicity of DDT and metoxychlor. This example shows that there is no definite dependence of substances' toxicity upon temperature.

Polychlorinated biphenyls (PCB) have, until recently, been widely used in industry as dielectrics, braking fluids and plasticisers. They are, in effect, mixtures of two-cyclic compounds saturated to varying degrees by chlorine. These compounds proved quite persistent and capable of building up along the food chain. The PCB built-up rates reach the values of 10^5-10^7. The PCB concentrations in samples taken form the Wisconsin River basin (USA) were up to 56 μg/l in effluents, 61 mg/kg in bottom sediments and 90 mg/kg in fish [12]. Fish fry had 4.6-8.8 mg/l PCB on the 60th day. Fish larvae are susceptible to 0.1 mg/l PCB.

Apart from these principal groups, attention of toxicologists is presently drawn to synthetic surface-active substances, water chlorination products, wastes of certain chemical production facilities, and radioactive substances.

Studies of the combined action of several substances is a special research problem. In practice, the combined effect of ions of several substances manifests itself normally more often than do the effects of individual substances. Possible combinations of toxic effects include antagonism (mutually weakening effects), synergism (the summary action is slightly weaker than the sum total of individual effects), additivity (the summary effect amounts the total of individual effects), and sensitization (mutual potentiation of individual ion actions)/5/. Depending on the ionic composition, various forms of interaction may reciprocally substitute for one another.

Diagnosis of hydrobiont intoxications employs a variety of indices.

The relative value of these indices for survival of organisms or communities may be different. It is quite impractical to attach identical importance to all credible changes in any functions. Considering this all indices may tentatively be divided into the main biological indices involving such properties as survival, growth, fertility and quality of progeny and secondary indices involving all other properties. The usefulness of secondary indices is subject to their proven qualitative or quantitative linkage with the main indices. The impact of a substance on characterizing the organism, a population a population or a community is the measure of its toxic action. As the notion and characteristics of a "normal" state of an organism have not yet been determined, its state or the index value in a model experiment may be taken as a guide. Such indices as modified gas exchange, growth rate and food intake are also important. These indices are reflected in some way or another in metabolism. Growth related metabolism is referred to as plastic metabolism. It includes the growth and renewal of tissues and the deposition of reserve substances.

Locomotion-related metabolism is referred to as energy exchange. The part of matter and energy that goes into the reproductive process is called reproductive metabolism.

Unfavorable environmental factors effect primarily plastic metabolism. The energy exchange may even increase in this case. Being dependent on plastic metabolism, reproductive metabolism is easily affected. When plastic metabolism is inhibited all the matter assimilated by an organism is expended to support its vital needs and functions. In most cases toxic exposure retards growth, irrespective of higher food intake. Formation of reproduction cells is inhibited. Ultimately, it results in lower productivity and size diminution of a population. Impairment of plastic metabolism may reduce the organism's tolerance not merely to anthropogenic factors but also to natural exposures.

Consequences of a disrupted biochemical process may cause structural or functional impairments. Some of them are used as indices of a particular type of impact. Behavioural and reflex reactions are also affected in a rather conspicuous and tangible manner.

Analysis of toxic effects on aquatic organism is complicated by polymorphism in their development. In such cases, different growth stages have to be studied separately. On the whole, early development stages in hydrobionts are more susceptible to exposure. In fish, this sensitivity increases in the following sequence: adults - roe - fry. The relative tolerance of roe is attributed to its retarded metabolism and specific permeability. Phenol sensitivity, however, grows with age. In embryonal development, young and adult individuals go through sensitive or critical stages.

Adaptation of hydrobionts to toxic pollution has to be discussed with special reference to the diversity of its manifestatioss: there are many ways in which organisms interact with their environment or respond to environmental changes.

Adaptation is defined as an organism's adjustment to external stress producing factors in order to abate the stress. The chemical composition of the environment is one of these factors. An organism may adapt itself to a modified chemistry of the envoronment within a broad range of values, with the exception of environmental changes brought about by natural calamities and certain anthropogenic impacts.

Although the possibility of adaptation has been proved its mechanisms and effectiveness remain unexplored. Generally, increased resistance of a population or of individuals to toxic contamination involves a sacrifice of valuable properties of aquatic organisms, causing, for example, a drop in fertility or unit size of a population. We are, therefore, unable, for the time being to count on the ability of the biocenoses in the water bodies to adjust to environmental contamination.

The ultimate goal of aquatic toxicology is to investigate the toxicological implications of pollution for aquatic communities. It is the survival of aquatic communities through maintaining good water quality and commercial productivity of water bodies that matters to man.

Preservation of water quality is assured by almost all hydrobionts, yet the major burden of water bodies - self-purification devolves upon groups of bacteria, fungi, protozoa, algae, and filtrators - crustaceans and mollusca.

In terms of productivity, the group of vegetative organisms (algae and higher aquatic plants) is singularly important. Although some species in the group cause enough trouble by their developmental outbursts and florescence, the group is nonetheless essential as a food source for all other hydrobiont groups, notably heterotrophs including feed and commercial organisms.

The various groups of aquatic organisms show well-established nutritional or trophic interrelations, representing a complex yet well-balanced system. Toxic agents are capable of causing a substantial restructuring o. the ecosystem.

Elimination of species or of their groups most sensitive to a particular exposure usually occurrs as an initial step of a biocenosis transformation. Eventually, these transformations lead to the degradation of aquatic ecosystems.

Thus we see that aquatic toxicology has to deal with toxic effects of a large number of pollutants on specific functions of different aquatic species and on entire bio-communities. Such a wide spectrum of goals necessitates employment of a great variety of research techniques. The choice of a method depends on the index to be studied.

Toxicity estimation may require employment of "instant" methods. One such technique is the "first test" suggested as early as 1913 /3/ adapted later for tother purposes/8/. The test procedure is as follows:

Six fish or 10 invertebrates are placed into a glassvessel with a solution of a toxic substance or diluted effluent. The frequency of solution replacement is dictated by the substance's stability or volatility. Records are made of survival, lethal times for 50 and 25 per cent of the organisms and their behavior (air swallowing, movements, turning to one side or overturning). The invertebrates used are Daphnia, Cyclopidae, and Oligochaete. The surveillance periods are 5, 10 and 20 days.

Results from acute experiments are only a source of data for estimating toxicity and forecasting possible effects of chronic exposures if a quantitative link between them is found. Credible inferences with regard to toxic effect can only be made on the basis of prolonged experiments with chronic exposure to agents.

The chronic investigation procedure requires the use of sample organisms from different groups of bio-communities at different development levels. The samples must be either pure cultures or those kept in the laboratory for two weeks before the experiment. The experiment involves several concentrations or dilutions differing from one another by a factor of 5 or 10.

The main processes or groups of organisms under study are as follows:

1. Self-purification. The overall activity of bacteria, fungi and protozoa is estimated. The bottles holding a toxic agent dissolved in 150 ml of river water at different concentrations are kept at 20°. After, 1, 3, 5, 7, 10, 15 and 20 days concentrations of O_2, ammonia, nitrites and nitrates in the samples are measured. The difference between the initial oxygen concentration and any other subsequent concentration is a measure of biological oxygen demand (BOD). Usually BOD on the fifth day (BOD_5) is used as the index. After filtration through filter No.2 direct count of cells is made according to the Rasumov method.

2. Primary output. Green algae are grown on Uspensky's medium (Chlorella and Scenedesmus) and blue-green algae on Fitzgerald's medium (Microcystis) in a luminostat at 3000 lx in 300 ml bottles. After 1,3,5,7,10, 5,20 and 30 days the cell count is made in Goryaev's chamber. The cells are evaluated for colour, condition, photosynthesis and respiration in Warbour's apparatus, and the quantity of chlorophyll A and B is measured. Higher plants (duckweed and waterweed) are grown under the regular insolation conditions in 150-200 ml dishes each containing

five bits of a plant. Measurements of the shoots' and rootlets' growth as well as of the lenght and number of blades are made every 5 days over a 30 days period.

3. Lower heterotrophs. Ten Daphnia are placed into glass bottles with 200 ml solution. Solutions are replaced every two or three days. The samples are fed daily with yeast or chlorella. Daily assessements are made of the number of live and young specimens, of eggs in the hatching chamber,,of ephippia and shed carapaces. The same applies to subsequent generations. Besides the initial generation, the first litter in every generation is kept under observation for thirty days. All subsequent litters are removed. Daphnia propagate mainly by parthogenesis. Under unfavourable conditions ephippia appear from which males are hatched. For Daphnia, the factors to consider are size, oxygen consumption, and cardiac rhythm.

For pond snails, ese factors are survival and reproduction; for bivalvular mollusca, survival and behaviour.

For chironomid larvae, account is taken of their survival, pupation, and emergence of imago.

4. Higher heterotrophs, including long-lived fish species, are studied stabe-by-stage. Egg fertilization is estimated in dishes. Two to three hours later the formation of embryonal disk and the onset of fragmentation is observed under a microscope. Fertilization percent age is assessed by the formation of 4 to 8 blastomeres. During the development period, the dates to be recorded include the emergence of the gastrula, the onset of cardiac output (rhuthm), hatching, survival of larvae, start of active feeding, and appearance of malfor-

mations.

Survival of small fry along with their general condition, pattern of movement and responses are recorded during 25 days. In this year's brood, their nutrition, respiration, growth, and increment of dry matter are watched for 30 days, as are two blood characteristics - blood count and hemoglobin content.

Even from this general account it should be evident that the proposed methodology is complex and labor-consumihg. Toxicity assessment under a full-scale programme takes, on average, three months. Two trends in aquatic toxicology methods have presently emerged. On the one hand, attempts are being taken to simplify and accelerate the procedure for obtaining response without detriment to reliability. On the other, increasing attention is being paid to standardization in order to assure comparability of results obtained under different conditions.

Each system of water use has its own set of regulatory requirements covering a broad range of different indices which include maximum permissible concentratioss (MPC) for various substances. The most stringent demands are posed by the healts and fishery standards. Their MPCs are lower than those for other types of water use. In the USSR the fishery MPCs have been developed for more than 300 substances. With a few exceptions, fishery MPCs are lower that health MPCs.

The limiting index in the fishery MPCs is toxicity under prolonged exposure. Organisms with short life-cycles provide an apportunity for evaluating long-term toxic effects. In the final analysis, the fishery MPCs are meant to preserve biological communities of water bodies rather than individual organisms. The MPC threshold for commercial fisheries is established at a deviation of major biological indices by more than 25 per cent. Experience has shown this level of deviation from the control to be the lowest statistically significant level for many indices. Not only does this curb inhibition, but also it curbs stimulation of some organisms. Stimulation of the growth of, say, blue-green algae or weedy organisms is obviously useless and even harmful.

The toxicity of a substance for which a fishery MPC has been established, is to be evaluated according to the above full-scale programme. The results are tabulated as shown in Table 1 /4/. The table gives maximum permissible concentrations for every index. The limiting index is the one the maximum permissible concentration of which is the lowest. Such concentration is taken as the MPC.

Comparison of selected fishery MPCs used in the USSR and the criteria recommended by the US Environmental Protection Agency [I] is presented in Table 2. The bioassays technique is introduced to perform current toxicological evaluation of water quality. The system is based on registration of hydrobionts's primary response to toxic impacts. In fact, the technique involves the substitution of a biological object for an analytical indicator. In any case bioassaying is no substitute for standardization but only a complement to it.

Development of bioassaying and standardization methods is a scientific challenge. On the one hand, excessively low limits may lead to unwarranted loss of financial and manpower resources. On the other, if the requirements are not stringent enough, pollution may trigger changes in biocommunities that can not be now properly assessed, but which are certain to be harmful to man in one way or another.

This short review of the state of the art of protection of living organisms in water bodies against toxic pollution shows that quatic toxicology is the most thoroughly explored area in ecotoxicology. The approaches, concepts and methods of aquatic toxicology may be used as a basis for advancing other fields of ecotoxicology and can contribute substantially to medical tocicology. Our efforts in the field are primarily prompted by the desire to protect human health and supply human needs.

REFERENCES

1. E.A.Veselov. Classification of efflients and components thereof by impact on water bodies and hydrobionts. In: "Toxicity Criteria and Methodological Principles of Aquatic Toxicology". MGU Press, 1971, pp.43-76 (in Russian).

2. S.A. Mileikovsky. The extent of oil pollution in the world ocean (review of publications). "Okeanologiya", 1979, 19, N 5, pp.829-834. (in Russian).

3. Ya.Ya.Nikitinsky, V.I.Dolgov. Report of Microbiol. Lab. Report of Interim Committee for Designing Measures to Protect Water Bodies in the Moscow Industrial Region against Pollution by Effluents and Disposals from Plants and Factories for 1912. Moscow, 1913 (in Russian).

4. Responses of Hydrobionts to Tin Organic Compounds. MGU Press, 1979 (in Russian).

5. D.L.Rubinstein. General Physiology. Moscow, 1947 (in Russian).

6. A.I.Simonov et al. Processes of Sea Water Self-Purification from Chemical Compounds. Trans. GOIN, 1978, 128., 61-63 (in Russian).

7. N.S.Stroganov. Progress of Aquatic Toxicology in the URSS. "Scientific Papers of Higher School. Biological Sciences". No.12, 1967, pp.7-21 (in Russian).

8. N.S.Stroganov. Methods for determining aquatic toxicity. In: "Procedures for Biological Investigations in Aquatic Toxicology". Moscow, Nauka, 1971, pp.14-60 (in Russian).

9. E.Heinisch, H. Paukke, H.-D.Nagel, D.Hansen. Agricultural

Chemicals in the Environment. Moscow, Kolos, 1979 (in Russian).

10. V.V. Khlebovich. Acclimatization of Animal Organisms. Leningrad, Nauka, 1981 (in Russian).

11. C.C.Butler. Introduction. In: "Principles of Ecotoxicology. SCOPE 12", ed by Butler, 1978, XIX-XXII.

12. J.J.Delfino. Toxic substances in the Great Lakes. Environ. Sci. and Technol., 1979, 13, No.12, pp.1462-1468.

13. L.T.Kurland, S.N.Faro, H.Siedler. Minamata Disease: the Outbreak of Neurologic Disorder in Minamata, Japan, and its Relationship to the Investigation of Seafood Contaminated by Mercuric Compounds. World Neurol., 1960, No.1, p.370.

14. D.R.Miller. General Considerations. In: "Principles of Ecoxicology. SCOPE 12". Ed by Butler, 1978, pp.3-9.

15. Quality Criteria for Water. 1976. US Environmental Protection Agency. Washington D.C., 1978.

16. J.-P.Raffin et al. Evolution sur trois années de quelques sites litteraux de Bretagne après pollution petrolium (Amoco Cadiz, 1978); Cahiers de Biologie Marine, XXII, 1981, pp.323-348.

Table 1

Permissible concentrations of thrimethyltinchlloride (TMOX), thriethyltinchloride (TEOX), thripropyltinchloride (TPOX) and triaminotinchloride (TAOX) for hydrobionts (mg 1) from [4]

Groups	Organisms	Indices and Duration of Experiment	TMOXI	TEOX	TPOX	TAOX
Bacteria	Saprophytes	Number of Syprophites cells	1	-	20	0.01
		BPK	1	1	20	0.001
	Nitrificators	Formation of NO_2	1	0.3	0.01	0.001
		"-" NO_3	10	0.3	0.05	0.001
Algae		Cells, quantity (30 days)	0.2	0.03	0.005	0.01
Macrophytes	Water-thyme	Plant survival (30 days)	2	-	-	0.001
		Increment in lenght	0.01	0.3	0.005	0.001
		Formation of side sprouts and total lenght	1	-	-	0.001
		Formation of roots and their lenght	0.01	-	-	0.0001
	Duckweed	Survival (26 days)	2	-	-	0.1
		Reproduction	2.0	0.03	0.01	0.001
		Roots, quantity	1	0.01	0.01	0.001
		Total roots length	0.1	-	-	0.0001

	Daphnia Survival (30 days)	0.01	0.01	0.001	0.0001
	Reproduction age	0.03	-	-	0.0001
	Fertility in three generations	0.01	0.01	0.001	0.0001
Crustacean	Molting (Shed carapaces)	0.01	0.01	0.001	0.0001
	Size fluctuation	0.01	-	-	0.0001
	Streptocephalus Survival (30 days)	0.02	-	-	-
	Reproduction age	0.01	-	-	-
	Number of laid eggs	0.01	-	-	-
	Percentage of births	0.01			
Fish	Leucaspius delineatus Survival (30 days)	0.1	0.1	-	0.001
	Carp Surlival: This year's brood (80 days)	0.05	0.01	0.01	-
	Weight change of two-year olds (120 days)	1	-	-	-
Perch	Embryonic state	1	1	-	0.01
	Survival of pre-larva	0.5	0.1	-	0.001
	Mutilation of pre-larva	0.1	0.1	-	0.001
Groundling	Embryonic state	5	0.1	0.01	0.01

Survaval of pre-larva	1	-	-	0.001
Multilation of pre-larva	0.5	-	-	0.001
Maximum permissible concentration (MPC)	0.01	0.01	0.001	0.0001

Table 2

Certain quality criteria for water suggested by the US Environmental Protection Agency in respect of hydrobionts and the USSR fishery MPCs (mg 1)

x - sea environment.

N°	Regulated substances	US criteria	Soviet MPC's
	Inorganic Substances		
1	Ammonium	0,02	0,008-1,2 (depending on the anions)
2	Iron	1	0.05^{x}
3	Cadmium	4.10^{-4}-0.012 (depending on water hardness)	0.005
4	Copper	1/10 of LC^{96}_{50} for local sensitive species	0.001 0.005^{x}
5	Nickel	1/100 of LC^{96}_{50} for local sensitive species	0.05 0.01^{x}
6	Mercury	5.10^{-5}	0.001^{x}
7	Lead	1/100 of LC^{96}_{50} for local sensitive species	0.1 0.01^{x}
8	Yellow phosphorous	10^{-4}	0
9	Chlorine	0.002-0.01	0
10	Chromium	-	0.001 Cr^{3+}
11	Cyanides	0.005-0,1	0,05
12	Zinc	1/100 of Lc^{96}_{50} for local sensitive species	0,01 $0,05^{x}$

	Organic Substances		
13	Aldrin	3.10^{-6}	0
14	DDT	10^{-6}	0
15	PCB	10^{-6}	0
16	Phenols	0,001	0,001
17	Oil and Lubricants	1/100 of LC_{50}^{96} for local sensitive species	0.001 0,01[x]

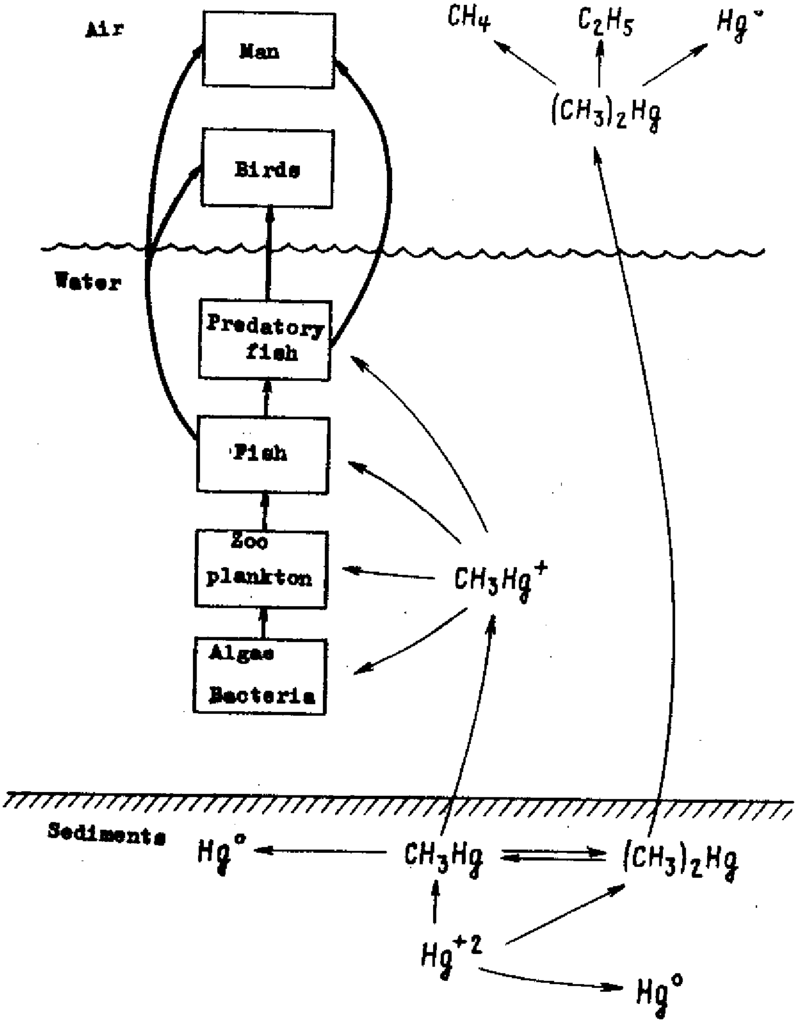

Air
Man
Birds
Water
Predatory fish
Fish
Zoo plankton
Algae Bacteria
Sediments
CH_4
C_2H_5
Hg°
$(CH_3)_2Hg$
CH_3Hg^+
Hg°
CH_3Hg
$(CH_3)_2Hg$
Hg^{+2}
Hg°

Fig.1

METHODS OF EVALUATION OF POLLUTANTS EFFECTS ON ECOLOGICAL ENVIRONMENTS

V.N. Maximov

Experimental investigation of combined effect of pollutants upon any biological system can be thought of as studying the function of several variables. Pollutants or toxicants should be considered as independent variables or factors; their levels should be varied according to a certain plan; and the system's response to this pre-planned combination of factors is usually described by a response function. The principles governing the conduct of multi-factor experiments are well-established (Nalimov, Chernova, 1965; Adler et al., 1976) and their detailed presentation is the subject of a special lecture course.

The multifactorial experiment carried out according to a statistically based plan can provide an answer to the question whether the effect of toxicants or pollutants upon a biological system is additive or non-additive. This remains valid, however, only as long as the combined effect is described in terms of just one factor of a given biological system. Clearly, when the impact of several pollutants on an ecosystem is studied in its entirety, the effect of each one can be described as a whole set of parameters each of which represents the response of a single ecosystem element (a population, trophic or topic group, etc.) to changes in pollution levels. It is imperative, therefore, to come up with a cumulative index which would combine individual responses of the ecosystem components into a single indicator of its state.

There are presently over a dozen different systems used to describe natural water quality with the help of hydrobiological indices. In fact, every European country uses its own system of water quality evaluation based on data of hydrobiont communities in various water bodies (Woodywiss, 1981). It ought to be stressed right away that, whenever water quality needs to be assessed irrespective of the requirements of specific users, it is the state of an aquatic ecosystem that is actually evaluated, though the concept is not clearly defined as a rule. A closer scrutiny of the systems and methods used to evaluate the status of aquatic communities makes it obvious, first of all, that the great majority of them are based on relative abundance data of particular species or their groups in the ecosystem. In other words, the state of an ecosystem is characterized using the species composition of the communities that inhabit it.

Functional characteristics data, such as productivity, destruction, and the circulation rate of biomass and biogenic elements in an ecosystem are much less used. The reason is that we still measure not the values we need but those which lend themselves to measurement. For example, abundance of fish in water bodies, i.e. populations of particular fish species has thus far defied exact estimation. Accordingly, the evaluation of water bodies for fish productivity relies exclusively on fish catches - although it has been known for a long time that the make-up of fish populations differs widely from the size, age and species composition of the fish catchable with modern fishing.

Here, incidentally, lies the difference between the experimental and modelling approaches to the studies of ecosystems. Model-building always assumes a dependence between the rates of processes and controlling factors, yet in most cases there seems to be no way of measuring the rates experimentally. All we can do, in effect, is to estimate the numbers of species in a water body, chiefly of small animals (plankton and meiobenthos) and microalgae. All the remaining values used in ecology have to be computed from the inputs of estimates thus obtained with the help of micromodels such as e.g. those describing the dependence of the breathing rate on body weight or exponential dependence of growth rate upon time. It seems, that primary productivity and respiration are the only exceptions being determined in bottle with chemical methods. However, this, too, amounts to the use of micromodels, not mathematical but mechanical, so to speak, since the bottle with plankton-containing water is called to serve as a model of the planktonic community in the water body of interest.

This is exactly why plankton or benthos data or biomass data derived from them are preferred in deriving most of the indices that describe the state of aquatic systems, for they are the most reliable and readily determinable indices.

Another characteristic of all the systems and methods used for ecosystem status evaluation is that they completely ignore statistical estimates. Nor has the problem of reproducibility and accuracy of such evaluations ever come to be debated until recently. The first steps in this direction were made only in 1977 during the USSR-UK research programme in the river Trent basin (Fretwell, 1981). This odd state of affairs can partly be explained by the fact that many of the indices or parameters now in use have been originally intended for the purposes other than evaluations of the state of ecosystems. Such are, e.g., widely known and frequently used diversity indices (Fisher et al., 1943, Mc Arthur, 1955, Margalef, 1957).

In his time A.Thieneman (1926) pointed out that any deterioration of conditions in a water body must bring about a reduction of biological variety which he viewed simply as the number of species living in the water body. His thinking was quite simple: in good conditions all the species inhabiting a given biotope live and reproduce; a worsening of the conditions causes the most sensitive species to die out or migrate. This means once the species have grown fewer in number, this has been brought about by deterioration of the environment. Regrettably, for all its simplicity, this line of reasoning is far from indisputable. To begin with, if some species disappeared from the community this can only suggest that these species above have been negatively affected, not that ecosystem as a whole has deteriorated. For example, increased salinity in a large river estuary following river flow regulation was shown to sharply reduce the diversity of the parasitic fauna of fish and birds there - but can it be looked upon as unfavourable for the estuarine ecosystem as a whole?

On the other hand, a large body of data is now available suggesting that diversity indices are much too insensitive to the changes in natural water quality. Without going into detail, let us refer to one statement from an article by W.M. Brown who is an experienced specialist with the Water Research Center, Great Britain. He said that it would be wrong to assume that a single factor or a group of closely related factors such as e.g. water chemical properties can be the only determinant of the "biotic state" of ecosystem diversity at a given time; a reverse process, i.e. using a certain measure of community diversity or the presence of certain species as an indicator of water quality as affected by pollution seems also unwise and unconvincing at best or erroneous at worst (Brown, 1977).

Another group of indices used to assess the impact of pollutants upon aquatic ecosystems, but not intended for the purpose, are similarity indices. They were suggested as a measure of similarity in the descriptions of communities or, simply put, lists of species. Their application to ecosystem status evaluation also relies on a fairly simple but not too pursuassive logic. Comparison of species composition in samples collected from two different sites in a water body and discovery of differences in certain indices are viewed as an indication of changes of the ecosystem status. If, in so doing, the two sites also differ by the level of pollution, it is deduced that the changes so identified are due precisely to pollution. Thus the similarity index whose magnitude is by definition a measure of similarity between two descriptions comes to be actually used as a measure of variation in the community status under the action of pollutants.

For the approach to be valid at least two conditions have to be met: first, the observed changes must be proved to be brought about by pollutants, and, secondly, that the variation of the species composition must be proportional to pollution level.

Though both these requirements are far from being trivial, neither has been experimentally verified, to the best of my knowledge. To this it must be added that such use of similarity indices poses the problem of their reproducibility and sensitivity, i.e. the metrology problem. A simple example will suffice to demonstrate its importance.

We had at our disposal a body of data concerning the species composition of phytoplankton, derived from two river lengths up- and downstream of a pollution source. At each stretch several parallel samples were taken so as to permit comparison of similarity of the samples collected at the same site with that of the samples derived from different sites. Clearly, the divergence of the similarity index from unity or total coincidence of the species lists for samples taken at one point, can be attributed only to random errors in the sampling method, non-uniform phytoplankton distribution in water, and errors in estimating the number of cells (when the similarity index accounts for species abundance).

Amongst similarity indices, very frequent use is made of Serensen's index:

$$SRN = \frac{2c}{a + b} ,$$

where:

c - is the number of species common for both descriptions;

a - is the number of species in the first description;

b - is the number of species in the second description

For the sample collected at the same river length (parallel samples) the range of Serensen's index values was from 0.52 to 0.92 with 95 per cent of the total of over 100 comparisons falling within the limits from 0.58 to 0.82. On the other hand, for the samples taken at different sites and known to have different species composition, owing to the river's significant pollution downstream of the pollution source, Serensen's index values ranged from 0.38 to 0.62 and 95 per cent of the values occurred within 0.40 to 0.58 (see Table 1).

Equally popular among ecologists is Chekanovsky's index, an analog of Serensen's one but taking into account the abundance of each of the species in the description:

$$CZK = \frac{2 \min (n_1; n_2)}{N_1 + N_2},$$

where:

N_1 and N_2 - are total numbers of individuals (cells, specimen) of all the species in the first and the second descriptions, respectively;

$(n_1; n_2)$ - is the sum of the least numbers of each of the species in the descriptions under comparison.

The similarity (or rather, dissimilarity) between the parallel samples was characterized by Chekanovsky's index values ranging from 0.58 to 0.82 (95 per cent of the values within 0.60 to 0.80), whereas for the samples taken from different sites the index took on values from 0.28 to 0.62 and 95 per cent of them were within 0.30 to 0.58 (see Table 2).

The divergence of the similarity index value from unity in parallel samples, due to errors in estimating the species number and abundance, can be termed a systematic error, by analogy with the well-familiar metrological concept applied to any measuring instrument. Because the entire variation scale of Serensen's and Chekanovsky's similarity indices fits between 0 and 1 we obtain a systematic error of the indices as degree-of-pollution measures representing on average 30 per cent of the entire scale. This alone is enough to call into question the suitability of similarity indices for estimating changes in natural ecosystems. Let us add that we performed a detailed analysis of eleven different similarity indices described in the literature and found no significant advantages in any one of them either in the size of systematic error or in the sensitivity to species composition variation. One more reservation is in order: all these estimates are strongly dependent on the number of organisms (phytoplankton cells in this case) counted during the determination of the species composition. In the example just discussed their number was 500-800 cells per sample, which is no different from their usual count during routine processing of phytoplanktonic samples. An increase of the cell count to 1500-2000 reduces the systematic error of the similarity indices to 10-15 per cent, a gain that hardly offsets a tripling in the amount of work involved in processing the planktonic samples.

Let us consider an index originally designed for water degree-of-pollution assessment based on the status of aquatic communities. This is the Pantle-Bukk saprobity index most commonly used in the USSR (Makrushin, 1974). It uses the so-called indicator organisms, with primary emphasis given to water pollution by organic substances. Data on the occurrence rate of the organisms in water bodies with different pollution levels are used to derive the so-called saprobic valency of an organism, S_i. When a sample is found to hold 'n' species with saprobic valencies S_i and relative abundance h_i, the saprobity index is defined as the weighted average:

$$S = \frac{\sum h_i s_i}{\sum h_i}$$

Frequently, abundance is measured in points whereby a rare occurrence rate in a sample is taken to be equal to I point, frequent occurrence - 3 points and massive distribution - 5 points. There are also more refined evaluation systems, based on the share of a given species in the total number of organisms in the sample. It is sometimes suggested to employ species numbers as a measure of abundance. However, this is not always possible, as e.g. in dealing with periphyton or zoobenthos. Then a saprobity scale is introduced, as follows: S = 1.0-1.5 for oligosaprobic waters; 1.5-2 for α -mesosaprobic: 2.5-3.5 for β -mesosaprobic; 3.5-4 for polysaprobic; and 4.0-6.0 for eusaprobic.

As experience in handling the system grew, its inadequacies became increasingly wident. The main one is its low sensitivity to ecosystem changes which may be brought about not only by increasing organic matter contents, but also by inputs of quite different pollutants, e.g. heavy metals or other toxicants. For example, the samples we have used in our metrological study of similarity indices had saprobity (determined from the species composition of the phytoplankton at the polluted river length) equal to 2.02 on average, ranging between 1.98 and 2.05 in parallel samples; at the stretch where water was known to be clean and suitable for drinking saprobity averaged 2.01, i.e. it hardly differed from saprobity at the polluted reach. It is to be recalled that even in terms of similarity indices the two areas were quite different in their phytoplanktonic species composition

It seems to be generally impossible to describe water as "good" or "bad" unless its uses are considered. Hence are the widely different quality indices for different types of water use. The choice of indices will also vary a great deal. For example, water suitability for irrigation emphasizes primarily total salt concentration, alkalinity, and ratio of individual cations. By contrast, water quality evaluation for use in paper industry attaches much greater importance to such indices as color index, concentrations of suspensions, iron, organic matter, etc.

With the set of water quality indices having been precisely determined, we can on the basis of the afore indices formulate a generalized criterion expressed by a single number. Most frequently the so-called "desirability function" (Adler et al., 1976, Maximov, 1977) is used for the purpose. The principle of plotting of this function implies that each individual indice y_i is attributed conventional value d_i varing from 0 for quite unsuitable value y_i to 1 at value y_1 which meets the requirements of "ideal" quality. Generalized desirability D is calculated then as the mean geometric value from desirabilities d_i:

$$D = \sqrt[n]{d_1 \cdot d_2 \ldots d_n}$$

Let us illustrate the point on the example of the data from F. Woodywiss' article (1977). His work compares estimates of a biotic index made at different lengths on the river Trent and some of its tributaries with the values of essential hydrochemical indices estimated at the same way stations. Woodywiss found good correlation between water quality evaluation in points of the biotic index (from 0 to 10) and certain hydrochemical indices, such as permanganate oxydability, dissolved oxygen concentration, and ammonium nitrogen content. Upon averaging the values of the indices for each of the observed biotic index values obtained over five years of surveillance, Woodywiss discovered that every value of the biotic index had a corresponding value of each of the above indices. Consequently, it is safe to assume for the Woodywiss biotic rating of 10 (the highest quality), to be correlative with desirability $d_i = 1.0$ - when every specific value of any one of the hydrochemical indices has, juxtaposed to it, the desirability value equal to the appropriate rating reduced, by a factor of 10. If, for example, an average five-year ammonium nitrogen concentration of 3 mg/l was observed in the water with the biotic index of 4, the concentration can be assigned a desirability value $d = 0.4$. The same magnitude of desirability can be set for permanganate oxidability equal to 8 mg/l and the dissolved oxygen concentration of 7 mg/l. Using this principle as a guide and the graphs from Woodywiss' paper as a basic input, we plotted graphs for the conversion of natural values of selected indices into their desirability values, assuming desirability $d = 1$ for dissolved oxygen concentrations above 11 mg/l and zero values for permanganate oxidizability and water concentrations of ammonium nitrogen. Under the approach, "ideal water" would be one that is oxygen-saturated and free from organic compounds and reduced forms of nitrogen. This assumption of course is fairly arbitrary but then it is common practice in constructing a desirability function to choose natural values which are considered to be a "inattainable ideal" as the unit of desirability.

We have computed specific desirabilities for 49 stations from the Woodywiss' data. Generalized desirability D values calculated from specific desirabilities and multiplied by 10 were found identical with the Woodywiss index in 34 cases and only in four instances did the desirability diverge from the index by more than two units. This is a very satisfactory data fit. It would be interesting to compare the values of particular desirabilities for each of the three indices of our choice with the value of the biotic index. Despite a clear-cut linear relationship between these values, as was to be expected from the method of their calculation, a more than two points difference is found in 10 cases if water quality is described by dissolved oxygen concentration alone in 9 cases if evaluated from ammonium N concentration data; and in 8 cases if the permanganate oxidability desirability values are used. One should evidently concur with Woodywiss in that the links between the biotic index and selected hydrochemical data are hardly reliable evidence. This is not, however, because the links are indirect in the character, but because 'well-being' in an aquatic environment "as seen" by the hydrobionts and its degree as defined by the biotic index depend on a broad spectrum of abiotic factors present, whereas a more or less close correlation between a factor's level and the state of the biocenosis exists only for each one of them taken singly. In essence, the advantage of the desirability function amounts to its ability, when actually applied, to estimate precisely an aggregate of factors and thereby to yield a more accurate assessment of the ecosystem status than would be conceivable with each factor taken separately.

Table 1

Variational Series for Serensen's Index

Index value for parallel samples from one river site (midclasses)	Frequencies	Similarity index values for parallel samples from two different river sites	Frequencies
0.525	1	0.375	2
0.575	8	0.425	22
0.625	27	0.475	50
0.675	63	0.525	52
0.725	37	0.575	30
0.775	14	0.625	6
0.825	1	-	-
0.875	1	-	-
0.925	1	-	-

Table 2

Variational Series for Chekanovsky's Index

Index values for parallel samples from one river site (midclasses)	Frequencies	Similarity index values for parallel samples from two different river sites	Frequencies
0.575	1	0.275	1
0.625	11	0.325	1
0.675	29	0.375	9
0.725	66	0.425	25
0.775	41	0.475	44
0.825	5	0.525	50
-	-	0.575	23
-	-	0.625	9

REFERENCES

1. Yu.P.Adler, E.V. Markova, Yu.V. Granovsky. Planirovaniye experimenta pri poiske optimalnykh usloviy (Experimental design in searching after optimum conditions). 2nd edition, Moscow, Publishing House "Nauka", 1976.

2. W.M. Brown. Riby kak indikatori kachestva vodi (Fishes as water quality indicators). In: Nauchnye osnovy kontrolya kachestva poverkhnosti vod po gidrobiologicheskym pokazatelyam. Leningrad, Gidrometeoizdat, 1977, pp 200-201.

3. F.S. Woodywiss. Bioticheski index of river Trent. Makrobespozvonochniye i biologicheskoye obsledovaniye (Biotic index of river Trent. Macroinvertebrates and biological investigation). In: Nauchniye osnovy kontrolya kachestva poverkhnostnykh vod po gidrobiologicheskim pokazatelyam. Leningrad, Gidrometeoizdat, 1977, pp 132-161.

4. F.S. Woodywiss. Sovmestniye anglo-sovetskiye biologicheskiye issledovaniya v Nottingeme v 1977 g (Joint Anglo-Soviet biological studies in Nottingam in 1977). In: Nauchniye osnovy kontrolya kachestva poverkhnostnikh vod po gidrobiologicheskim pokazatelyam. Leningrad, Gidrometeoizdat, 1981, pp 117-189.

5. A.V. Makrushin. Biologichesky analiz kachestva vody (Bioassaying water quality), Leningrad, ZIN AN SSSR, 1974.

6. V.N. Maximov. Spetsificheskiye problemy izucheniya kombinirovannogo deistviya zagryaznitelei na biologicheskiye sistemy (Specific problems of study of combination effect of pollutants on biological systems). Gidrobiologichesky zhurnal (Hydrobiological Journal), vol. 13, No.4, 1977, pp 34-45.

REFERENCES (continued)

7. V.V. Nalimov, N.A.Chernova. Statisticheskiye metody planirovaniya extremalnikh experimentov (Statistical methods of experimental design), Moscow, Publishing House "Nauka", 1965.

8. G. Fretwell. Issledovaniye vliyaniya metodov otbora prob makrobespozvonochnikh na otsenku kachestva vod (Effect of macroinvertebrates species selection methods on water quality assaying). In: Nauchniye osnovy kontrolya kachestva poverkhnostnikh vod po gidrobiologicheskim pokazatelyam (Scientific bases of surface water quality monitoring by hydrobiological indices), Leningrad, Gidrometeoizdat, 1981, pp 190--203.

9. Fisher R.A., Corbett A.C., Williams C.B. The relation between the number of species and the number of individuals in a random sample of an animal population. "Journal of Animal Ecology", vol. 12, 1943, pp 42-58.

10. Mc Arthur R.H. Fluctuations of animal population and measure of community stability. "Ecology", vol. 36, No.7, 1955, pp. 533-536.

11. Margalef R. La teoria de la information in ecologia. "Mem. Real. Acad. Cienc. Artes Barcelona", vol. 32, 1957, pp 373--449.

12. Thienemann A. Limnologie. Jedermanns Bucherei, Breslau, 1926

ENVIRONMENTAL POLLUTION: ITS ECOLOGICAL CONSEQUENCES AND MONITORING

F. Ya. Rovinsky

The last few decades saw the emergence of a global concern about the protection of human health and nature from the adverse effects of economic activities. At the beginning, attention was focussed on industrial workers who constituted the most vulnerable group. Later on, attention was increasingly paid to consequences for people and the environment in the vicinity of pollution sources. There was a growing awareness of the fact that the scale of the impact was constantly growing and assuming international proportions.

To manage the problem it is necessary, first of all, to identify sources of pollution, estimate their scope and size, and understand the pathways of pollutants into the environment.

For ease of discussion, it would be advisable to separate the vast diversity of anthropogenic pollutants into three large groups:

- gaseous substances that enter the environment to act there primarily in the gas phase;
- heavy metals, i.e. chemical elements with a heavier-than-sodium atomic weight and a specific weight of over 5 g cm^3;
- organic substances, i.e. products of processed natural organic substances or synthetic products; many of them do not exist in nature and natural systems have not therefore become adapted to them in the course of evolution.

The first group of substances includes sulfure dioxide, nitrogen oxides, carbon monoxide, fluorides, chlorine, hydrogen sulfide and ozone. Closely allied to this group are emissions of dust which exist in the atmosphere for a long time as suspended particles.

During 1970-1980 the world's total emission of SO_2 increased 1.4 to 1.5 times, at the annual growth rate of 5 per cent, and amounted to over 150 million t/y; for NO_2 the figure was 27 million t/y and for dust - 83 million t/y.

Automobile transport plays an important role in the total atmospheric pollution. The world's 200 million or so cars release more than 200 million tons of CO annually. In the USA, 75 per cent of the CO pollution is associated with automobile transport; in Europe the figure is somewhat lower - 25 to 50 per cent.

The world's total annual discharges of Cl and Br are estimated at 4200 and 117 thousand tons respectively.

The second group of pollutants - heavy metals - includes, by definition, over 70 elements. However, considering the magnitude of their anthropogenic influx and the ab
in natural media and food chains, some 10 heavy
that pose the greatest risk - Hg, Pb, Cd, As, V, Sn, Zn, Sb, Cu, Mo, Co, Ni - and some other metals. Of these only the first four are of particular importance for the biosphere and man because of their universal distribution. Though equally toxic, the other elements have a more localised negative impact.

The burning of fossil fuels, such as coal, petroleum products, etc., for energy production is one of the most important anthropogenic sources of heavy metals in the environment. Emissions from this source are much larger than releases immediately associated with the mining of heavy metals. For Hg, As, Cd and Co, for example, this excess is 3 to 8 times.

The main source of Pb emissions into the atmosphere are exhaust gases. Some 10 to 15 years ago the Pb content in petrol amounted to 0.5 - 0.8 g/l, with up to 25 per cent of the world Pb production going there. From the exhausts, about 80 per cent of lead passes directly into the atmosphere, generally in the form of fine particles less than 1 μ in size, that enter the lungs and are deposited there. Today in most countries the Pb content in petrol is 0.15 g/l, yet motor transport still accounts for over 90 per cent of the total Pb pollution. Since the 1920's more than 5 million tons of Pb have been released into the atmosphere.

A substantial additional influx of Hg results from such "innocent" activities as land plowing, stripping and mining operations and drilling that enhance natural Hg diffusion through the earth's surface. This alone has doubled and tripled the amount of Hg released into the atmosphere from the earth's interior.

In the first group of pollutants it is necessary to examine organic substances of anthropogenic origin. These are, primarily, petroleum hydrocarbons, various pesticides and, above all, the most persistant organochloric compounds (DDT with its metabolites, HCCH and others); polychlorobiphenyls (PCB), 3,4- benzpyrene, an active carcinogen; and some other chemicals.

DDT applications have started to rapidly multiply since 1940 when its strong insecticidal properties were recognised. The total amount of DDT used until 1970 is estimated at 2 to 4.5 million tons. In 1970-1973, by the time the adverse consequences of DDT had come to light, its use was banned in some countries (the USSR, Sweden, Finland, etc.) and heavily limited in others (the USA, Brazil, etc.) DDT is still used in India, Egypt, Pakistan, Israel, Italy, Greece, Spain and countries of the southern hemisphere.

Over a thousand different pesticides are produced in the world, and 300 of them are most widely used. Their production totals over 130 million tons a year. Until 1970, the United States produced two thirds of the world's DDT output and exported more than 10 per cent of the amount.

Petroleum products and their derivatives constitute another important source of organic pollutants, with oil processing and petrochemical industries accounting for more than 90 per cent of their emissions into the atmosphere. However, there are still no estimates of the total world emissions. The hydrosphere suffers the worst from this kind of pollution. In 1970-1975, six to ten million tons of petroleum products went annually into the World Ocean, with 10 per cent contributed by the influx from the atmosphere.

3,4-benzpyrene, a polycyclic aromatic hydrocarbon, is strongly carcinogenic. It is formed during various thermal treatments of organic materials and incomplete fuel combustion. It has not been possible so far to assess its total anthropogenic release into the environment but there is no doubt that benzpyrene is permanently present in the atmosphere, sweet and sea water, soil and food.

There is no doubt that envoronmental pollution has a direct and negative impact on human health. Different pollutants enter the human organism in different ways, affect different organs and tissues, and generate a wide range of diseases and changes in human behabiour. The most vulnerable groups are children, the sick and the aged.

Acute respiratory diseases are caused by sulfur compounds (SO_2, H_2SO_4, sulfates) present in the polluted atmosphere of many large cities. Prolonged exposures to even relatively low concentrations of SO_2 increase mortality rates among cardiovascular patients. The effect of NO_2 changes also the respiratory functions of the lungs. CO has an especially noxious effect on humans. Upon entering the blood stream, it blocks the transport of oxygen by forming a compound with hemoglobin - carboxyhemoglobin. A 2-5 per cent concentration of this substance in the blood produces stable disturbances of psychomotor functions, 10 per cent seriously hinder the oxygen supply, and 40 per cent and more result in a coma and death. Compounds of F, Cl, HCl and a number of other substances produce a strong irritant effect on the mucous tissue of the eye and respiratory organs. Prolonged exposures result in pneumonia, bronchitis and other diseases of the lungs. A specific type of air pollution is photochemical smog.

Heavy metals that enter the human organism with air, water and food also have a highly toxic effect. Pb affects mainly the nervous and hemogenic systems as well as the gastroenteric system. Cd intake also entails serious consequences.

The influence of excessive amounts of Pb and Cd on the frequency of cardiovascular diseases has been identified although its mechanism remains unclear. As, Cr, Zn, Cu, Ni, Se, Ba and many other metals also pose health hazards and are present in excessive amounts in the environment, human organs and tissues in the vicinity of relevant industrial facilities.

Organochloric and organophosphorus pesticides enter the human organism mainly with food and water. As DDT progresses along food chains its concentrations begin to grow and the human organism gradullay accumulates these compounds, mostly in fatty tissues.

Benzpyrene is one of the most potent carcinogens emitted into the environment by anthropogenic sources. Exposure results in various forms of cancer: skin and lung cancer, cancer of the digestive tract and other internal organs.

Nitrozoamines form another group of carcinogens that are virtually absent from nature. They are formed directly in the stomach when nitrites react with different amine derivatives. Nitrites enter the human organism with food (food additives) and primarily with water.

Compared with the impact of pollutants on humans, the effect of pollutants on the environment and animals (including test animals) is not so clear although many effects are indisputable.

The SO_2 damage to the green parts of plants has been known for a long time. It consists mainly in inhibiting photosynthesis. With high concentrations of SO_2 in the air (above 0.5 ppm) necrosis takes a relatively short time to develop in leaves and plant growth is retarded or completely arrested. Sulfur compounds are capable of accumulating in tissues and interfering with enzymatic activity. The impact of SO_2 on higher vegetation is traceable even at relatively low background SO_2 concentrations in the air (about 10 $\mu g\ m^3$). Direct damage to plants from nitrogen oxides is normally observed only in cases of their high concentrations in the air, as in highly industrialised areas. A considerable injurious potential for plants inherent in fluorides and chlorides causes necrosis and chlorosis of leaves. The impact of HF on vegetation is significantly multiplied in the presence of H_2SO_4. Co is low-toxic to plants. Among the gaseous substances, oxidising agents O_3 are capable of inflicting the greatest damage. Plant damage becomes substantial already at O_3 concentrations in the air equal to 0.16 mg m^3.

The impact of air pollutants extends also to agricultural crops and cultivated plants. US estimates put the annual damage to agricultural crops at 85 million dollars, of which 78 million dollars is accounted for by the action of photo-oxidants, including 40 million dollars in losses of cotton yields, and 3-4 million each in losses due to the effect of SO_2 and fluorides. For ornamental plants, the damage amounts to 46 million dollars, of which 43 million is attributed to photo-oxidants and 3 million to SO_2.

Heavy metals affect plants primarily by hurting their root system. Excessive concentrations of heavy metals (Pb, As) in soils, for example, near mining and metallurgical plants, impede natural recovery of the vegetation cover. Pb, As, Cu and Co salts and those of other metals are capable of reducing or even inhibiting root growth.

Different plant species show different sensitivity to toxic exposures. Coniferous trees, for example, are almost twice as sensitive as decidous species. Mosses and lichens exhibit extraordinary sensitivity. That is why the variety of lichens has been drastically reduced in cities and their environs.

In addition to land vegetation, pollutants affect aquatic vegetation. As with lichens and mosses, algae accumulate toxic substances such as heavy metals, DDT, PCB and others. Even negligibly low concentrations of these toxicants are enough to suppress photosynthesis and growth in algae. Petroleum hudrocarbons are very strong toxicants of this kind. The sensitivity of algae species to the impact of petroleum products may vary by a factor of several thousand - an effect closely related to primary productivity.

Toxicity of pollutants also harms animals and birds as well as the inhabitors of fresh and sea water. In most cases, this occurs through the accumulation of the toxicants in the organisms. The higher a given species is located in the trophic pyramid, the larger, as a rule, the accumulation of toxic substances and the stronger their toxicological effect.

A specific type of toxic environmental impact comes as a consequence of the formation and fall-out of acid rains. Under normal conditions, their pH content is about 5.3 to 5.7. Observation data over the past decade frmm North America and Western Europe suggest a marked shift of the index to the acid area. The rains have, on the average, a PH close to 4 but there are some with pH of 2 to 3. The phenomenon is caused by the conversion of SO_2 and NO_2 into the corresponding acids. The processes take place in the atmosphere with the result that acid rains fall out far from the emission sites of sulfur and nitrogen oxides.

The ecological consequences of chronic acid rain precipitation vary a great deal. This phenomenon is associated with the observed slow-down of forest growth and, in some cases, even their direct injury. Young plants are particularly vulnerable to acid rains. Heavy influence of acid rains has been registered in aquatic ecosystems.

Any assessment of the state of the environment should be based on some criteria that characterise its critical or permissible states. Maximum allowable concentrations (MACs) of noxious substances in the natural media, that are developed chiefly in relation to humans, constitute today the most widely used single criterion for assessing the quality of air, fresh and sea water, and soils. In some countries such indicators are called environmental quality standards. Irrespective of the limiting toxicity factor of a given substance (toxicological, sanitary or organoleptic), its MAC is based on the concept of creating the most favourable conditions for the life of a given organism.

What is normally meant by an MAC is a concentration of a chemical compound whose daily impact on the human organism over a prolonged period of time does not cause any pathological changes or diseases as detectable by the available methods, and does not disturb man's biological optimum (e.g. the appearance of unpleasant odours or other undesirable organoleptic characteristics of the air and water).

At present, the Soviet Union has MACs for 145 substances and their 20 combinations in the atmosphere; for almost 500 substances in the ewater used for dringking and economic purposes, and for 32 substances in sea water. In addition, NACs have been established for 60 substances in the ewater of fresh water basins and seas used for fishing.

Most countries have instituted national systems for monitoring the state of the environmental and special government agencies have been set up to formulate policies and carry out specific activities.

The Soviet Union has set up and operates its National Service for Surveillance and Monitoring of the Level of Pollution in the Natural Environment and Early Warning of Abrupt Changes in the Pollution Levels. With the enhancement of measures designed to protect the natural environment in the USSR and to manage its natural resources, the role of information about the state of the environment becomes increasingly important. Monitoring environmental pollution and discharges and setting standards for pollution sources cnnstitute at present the principal realistic instruments for regulating the state of the natural environment and reducing its pollution.

The Soviet Union's National Service performs the functions and fulfils the objectives of a nation-wide system for monitoring environmental pollution. Its principal goals include:

- surveillance and monitoring of the level of pollution in the atmosphere, inland waters and seas, and soil, according to physical, chemical and hydrobiological parameters, with a view to ascertaining the distribution patterns of pollutants in time and space, assessing the state of the natural environment, and identifying the sources of pollution;

- providing agencies and organisations concerned with systematic and urgent information about changes in the levels of environmental pollution and with forecasts and warnings about possible changes in these levels.

Such information provides the basis for preparing materials needs for environmental protection and management of natural resources; for designing industrial plants and hydroengineering projects; for urban planning and locating large industrial and agricultural complexes.

In addition to its network of observation stations located in the areas prone to immediate anthropogenic impacts, the National Service includes base and regional stations responsible for background observations in regions to which pollutants can spread only because of their global distribution (base stations) as well as in intermediate regions where pollutants arrive by way of local migration (regional stations).

Thus, structurally, the National Service incorporates the following subsystems: monitoring of pollution sources; monitoring of air pollution; monitoring of inland water pollution; monitoring of sea water pollution; monitoring of soil pollution; and background monitoring (biosphere reserves, and regional and base stations).

Inland water pollution (rivers, lakes and water reservoirs) is closely linked with the problem of fresh water supply. It is no secret that in a number of countries, and in some regions of the USSR, there is not enough fresh water for agricultural and industrial uses, and, in some cases, for community services; in this situation the problem of water quality assumes special importance.

At present, the stationary observation network comprises 4,000 points covering over 1200 bodies of water across the USSR.

Soil and sea pollution monitoring covers respectively all major agricultural zones and inland seas and the seas adjacent to the USSR.

In conclusion, it is necessary to emphasise that a drastic reduction of toxic emissions into the environment, followed by their total elimination, is the only effective way to combat environmental pollution and offset its adverse economic consequences. This is also imperative for the management of natural resources, because many substances are now a valuable resource whose importance is growing due to the depletion of mineral resources. Their diffusion in the environment represents not only a risk for human health and nature but also a waste of the world's wealth.

The ways to abate the emissions are well-known. In a longer term, one of the ways will be a transition to low-waste and non-waste technologies. This is a radical, though rather costly, enterprise. Prior to that,it would be wise to systematically monitor the state of the natural enviroment and impose standards on environmental pollutants as a means of optimising the interrelations between nature and society.

REFERENCES

L: Yu.A. Izrael. Ekologia i kontrol sostoyania prirodnoi sredy (Ecology and Monitoring of the State of the Natural Environment), Leningrad, Gidrometeoizdat, 1979.

2. Yu.A.Uzrael, A.V.Tsyban. Problemy monitoringa ekologicheskikh posledstviy zagryazneniya okeana (Problems of Monitoring Environmental Impacts of Oceanic Pollution), Leningrad, Gidrometeoizdat, 1981.

3. Yu.A. Izrael, N.K. Gasilina, F.Ya. Rovinsky, L.M. Filippova. Osushestvleniye v SSSR sistemy monitoringa zagryazneniya prirodnoy sredy (Implementation of a System of Monitoring Envoronmental Pollution in the USSR), Leningrad, Gidrometeoizdat, 1978.

4. F. Ramad. Osnovy prikladnoy ekologii (Fundamentals of Applied Ecology). (Transl.from French), Leningrad, Gudrometeoizdat, 1981.

5. Globalny balans DDT v biosfere (Global DDT Balance in the Biosphere), A Review, Obnisk, 1978.

6. Globalny balans svintsa v biosfere (Global Lead Balance in the Biosphere), A Review, Obninsk, 1978.

7. Globalny balans rtitu v biosfere (Global Mercury Balance in the Biosphere), A Review, Obninsk, 1978.

8. Mikroelementy v atmosfere fonovykh rayonov sushi i okeana (Microelements in the Atmosphere of Background Regions of the

Land and the Ocean), A Review, Obninsk, 1978.

9. Vlianie izmeneniy khimicheskogo sostava sredy na rost rasteniy (Impact of Changes in the Chemical Composition of the Environment on Plant Growth), A Review, Obninsk, 1982.

10. Probley ekologicheskogo monitoringa i modelirovaniya ekosistem (Problems of Ecological Monitoring and Ecosystem Modelling), Leningrad, Gidrometeoizdat, 1978-1981, Vol. I, II, III.

11. Kompleksny globalny monitoring zagryazneniya okruzhaushey prirodnoy sredy (Integrated Global Monitoring of Envoronmental Pollution). Proceedings of International Symposium, Riga, USSR, December, 12-15, 1978, Leningrad, Gidrometeoizdat, 1980.

BIOINDICATION OF FRESH WATER POLLUTION

M.M. Telitchenko

The XXXY UN General Assembly declared 1981-1990 "The International Drinking-Water Supply and Sanitation Decade". This was preceeded by the UN Conference on Water Resources (Mar del Plata, Argentine, 1977) which stated that about one billion people suffer from the deficit of pure water on the Earth, which takes, the daily toll of 25 thousands human lives. Even in such a highly industrialized country as the USA twenty five major epidemics of aquatic etiology - gastroenteritis, dysentery, infectious hepatitis and lambiasis - involved thousands of human casualties within the period from 1971 to 1975. That is why, a reliable information about sanitary-hygienic state of natural waters is of a great importance. In his studies Soviet Academician V.I. Vernadsky considers water to be a bioinhabited body, i.e. its qualities are formed by hydrobionts. In this case biological adequacy of water should obviously be regarded as the main quality of the water being a product and an inhabited medium (18). Organisms only can supply reliable information about the biological adequacy of water.

A.Müller and F. Kohn in 1869-1870 published their works in Germany showing conclusively the major role of aquatic organisms (hydrobionts) in the transformation of pollutants. In 1875 Ferdinand Kohn, a botanist, was the first to subdivide waters into three groups according to the degree of their pollution and described the organisms characteristic for them. Since then the concepts of the involvement of hydrobionts in water purification and the assessment of water quality have acquired a firm scientific foundation. Major contributions to this were made by Metz and the research performed by the Royal Institute for Evaluation of Drinking and Sewage Waters, founded in Berlin in 1901. Its leaders, botanist R. Kolwitz and zoologist M. Marsson designated the organisms living in polluted waters as saprobionts (from the Greek *sapros* - rotten and *bios* - life). They found three distinct phases to exist in the self-purification of a river - contamination zones inhabited by three groups of organisms.

Polysaprobic (p) - the zone of microbiological reduction of organic pollutants, inhabited by polysaprobic organisms.

Mesosaprobic (m) - the zone of starting oxidization, inhabited by mesosaprobic organisms. Finally, the third zone, where the oxidation of organic matter is completed. Called *oligosaprobic* (o), it is inhabited by oligosaprobic organisms. The purest waters of mountain lakes, springs, etc. inhabited by katharobionts (from the Greek *Katharos* - pure) are often distinguished as a separate class.

The authors of the system understood saprobity as the ability of organisms to live in water contaminated by organic substances x).

Following the publication by Kolkwitz and Marsson in 1908 of an extensive list of vegetative and in 1909 - of animal indi-

---

x) At the International Symposium in Praque in 1966 the concept of saprobity was transformed. It was redefined to mean the sum of metabolic processes opposite to the formation of primary products, that is the sum of the processes involving a loss of potential energy of the water system (38) cator organisms, the sanitary-biological analysis of water quality found wide application in the national economies of European countries (1).

Sanitary-biological studies of water bodies acquired an especially great scope after the 1917 Great October Socialist Revolution when scores of institutes and universities joined in the effort (19, 20).

Rapid industrial and urban development coupled with a wide use of chemicals in agriculture and everyday life intensified the pollution of natural waters by not only domestic but also industrial sewage. In this new context the deficiencies of the Kolkwitz-Marsson system, widely accepted in European countries, became particularly obvious.

A prominent Soviet hydrobiologist, Professor V.I.Zhadin repeatedly noted that the Kolkwitz-Marsson system "does not work anymore beyond the Urals" (5). Therefore, there is a need in a universal system of saprobity that would permit evaluation of natural water pollution both by domestic and industrial effluents (6). In this connection, the Czech researcher V. Sladeček (15) proposed a "universal" system for water quality evaluation, consisting of the following zones:

1. Katharobic (K) - pure ground, mineral or artificially prepared drinking water.

2. Lymnosaprobic (L) - the quality of these waters can be estimated in terms of the Kolkwitz-Marsson saprobity scale (the major portion of natural waters).

3. Eusaprobic (E) - sewage waters containing biochemically decomposed organic substances. These are subdivided into isosap-

robic (i), the habitat of infusorians; metasaprobic (m), of colorless flagellates; hypersaprobic (h), of bacteria and fungi; and ultrasaprobic (u), abiobic.

4. Trans-saprobic (T) - sewage or surface waters that do not undergo biochemical decomposition. These include waters of three types of quality: a - antisaprobic, with toxic substances; r - with radioactive substances; and c - cryptosaprobic, artificially heated or cooled, containing suspensions, etc.

The scheme does indeed seam to be a truly universal one, but it does not solve the main problem of how to simplify quality assessment for the bulk of natural waters (L), how to decide on the state of their biological adequacy. This is because, for this one purpose, the author still adheres to the Kolkwitz--Marsson system, while all living scales used to evaluate the state of the environment are much too cumbersome. This is exemplified by the biological system to evaluate the state of farming lands, proposed by L.G. Ramensky (14) or of fresh waters, by O.P. Oksiyuk and V.N. Zhukinsky (7). Besides, the results of evaluating the water quality as well as the quality of agricultural lands have to be numerically or graphically represented, otherwise they cannot be used in national economy.

In order to obtain morpho-taxonomic information on water purity using the Kolkwitz-Marsson scale in numerical and graphic form the following concepts were introduced: indicatory significance (saprobity index) - S - for indicator organisms in accordance with the degrees of their saprobity (O = 1; β = 2, α = 3 and p = 4); and the relative number of specimens of each indicator species - h (from 1 to 9).

Number of specimens of one indicator species in % of the total number of all specimens	Value of the frequency of occurrence - h
1	1
1-3	2
4-10	3
10-20	5
20-40	7
40-100	9

Using these values, Pantle and Bukk in Czechoslovakia proposed that water quality should be assessed in terms of saprobity index - S:

$$S = \frac{\sum Sh}{\sum h};$$

We see that S is a simple arithmetic mean of the occurrence frequency rates and saprobity values (0-4) of the indicator species belonging to a certain ecological group - benthos, plankton, periphyton, or nekton. The overall saprobity index is the arithmetic mean of saprobity index values for several ecological groups (29).

G. Liebmann (27) proposed that water quality in a source should be represented graphically (in plan).

Water quality evaluation with the help of saprobity index has a disadvantage in that it fails to account for the ability of many organisms to live in waters belonging to different zones (stages) of saprobity (x, e, b, a, p), as well as the dissimilar degree of saprobity in individuals of even the same species, but found at different points of their range. To fill the gap Zelinka and Marvan (33) introduced the concepts of saprobic valency of an indicator and the species indicator weight "j". Saprobic valency of an indicator shows the saprobity stage in which it occurrs. Saprobic valency values for different saprobity stages are calculated on the assumption that 100% of the indicator species organisms are equal to 10 and that its value in each stage will be a fraction of 10. "j" is estimated in points from one to five. If a species occurs in one saprobity stage its j = 5; in up to two stages, j = 4; in up to three stages, j = 3; in up to four stages, j = 2 and in up to five stages, j = 1. The number of specimens of the indicator species, h, is also taken into account. It is expressed as an absolute number or the percentage of specimens in an assay. In practice, the computation sequence is:

$$\bar{x}/\bar{o}, \bar{\beta}, \bar{\alpha}, \bar{p}/ \quad A = \frac{\sum\limits_{i=I} \bar{x}_i \cdot h_i \cdot j_i}{10} \quad \text{or } A = \frac{\sum\limits_{i=I} \bar{x}_i \cdot h_i \cdot j_i}{\sum h_i \, j_i} ;$$

The degree of water pollutior is determined from the greater numerical value of the corresponding saprobity stage (0, β , α , p). The Zelinka-Marvan method is the most advanced modification of the Kolkwitz-Marsson system. Its application is, however, limited by the fact that the "saprobic valencies" and "indicator weight" (i) of representative organisms are not the same in different geographical zones. Moreover, the method is laborous and requires a good knowledge of flora and fauna. For a more detailed account of the morpho-taxonomic methods one can recommend, the review given in the lecture made by Persun and de Pau (30).

With a view to a faster and simpler biological evaluation of water quality, ecological-physiological indices were proposed.

It is well known, for example, that the number of hydrobiont producers increases and that of consumers and reducers decreases with progressing self-purification of water.

Based on that, Gabriel (25) proposed to use the pollution index in estimating water quality:

$$i = \frac{2p}{R + c}$$

where:

p - is the biomass of producers;

R - is the biomass of reducers and

c - is the biomass of consumers

For a crude estimation of water quality large taxa are often used as its bioindicators. Goodnight and Uttlay (26), e.g., suggest determining the sanitary condition of rivers by the number of oligochaeta present in them.

I - good sanitary condition of a river, with the oligochaeta accounting for less than 60% of the total number of benthic organisms;

II - questionable condition of water, with oligochaeta from 60 to 80 per cent;

III - a polluted river, oligochaeta in excess of 80%

Y.V. Balushkina found that river pollutants change the numerical ratio between the chironomid larvae of the Chironominae, Orthocladiinae, and Tanypodinae subfamilies, with the orthocladiinae larvae dominant in pure water and the tanypodinae - in contaminated water. For water purity indication Y.V. Balushkina proposed the following index:

$$K = \frac{a_t + 0.5\, a_{ch}}{a_{or}} ,$$

where:

a_t, a_{ch} and a_{or} - are the numbers of larvae of each subfamily (4).

Since the species diversity of a hydroecosystem declines with an increase in its pollution, some investigators suggest that species diversity index should be used to estimate the water quality. Margalef (28), e.g., in the belief that the total number of species is proportional to the logarithm of the area they live in, proposed the following equation as a measure of species diversity and, thereby, of water purity evaluation:

$$d = \frac{S - I}{\mathrm{Ln}\ N} ,$$

where:

S - is the number of species and

Ln N - is the natural logarithm of the number of individuals.

Index d acquires its maximum value when all specimens in an assay belong to different species ($S = N$) and equals zero when they all are of the same species ($S = I$). Methods have been proposed based on information theory. For example, sequential comparison index (S.C.I.). The method is based on a modification of the principle of test assays and on the group theory (24). The analyst is required to be able to recognize clearly the color, shape and size of the object. He has to compare the observed organisms against the conventional criteria (images) from the table. The observed organism resembling the conventional image is indicated by a plus, if there is no resemblance - a minus. In this way the number of groups and of individuals in them is assessed.

The number of species of the organisms similar and dissimilar to the conventional images is then determined, and the index is found from the formula:

$$\text{S.C.I.} = \frac{\text{N groups}}{\text{N individuals}} \quad \text{N tests}$$

It is easily seen that with a decrease in species diversity, e.g., the effect of pollutants, the value of the index will be less than unity.

The hypothetical nature of these methods should, however, be stressed. It is known, e.g. that species diversity is minimal in pure spring and heavily contaminated waters. Besides, the method yields data on the magnitude of pollution but says nothing about its specificity.

Evidently, in order to increase the accuracy of water quality indication, the merits of all the methods described above should be integrated within a single indicator system. Woodywiss' system, from the Trent River inspection in England (32), should be regarded as the best attempt of this kind. The system postulates that, with increasing water pollution, the diversity of hydrobionts will decrease and the only surviving indicator organisms will be the ones best-adapted to pollution.

The determinative system of Woodywiss characterizes the extent of water pollution with large taxa - families, orders and classes of benthos named "groups". This extends the geographical boundaries of its application. But, in order to enhance the table's indicator capability for specific regions, its structure also incorporates the region - specific indicator species. As a result, such indicator species as Baetis rodani, Asellus aquaticus, Chironomus thummi have to be locally substituted by "equiecological" indicator species, i.e., those occupying a similar ecological niche in the region studied. This should stimulate research aimed at ascertaining and describing the appropriate indicator species in different geographical regions. The Woodywiss biotic index values fall from 10 to 1 as water pollution increases. Regrettably, the system is primarily designed to estimate the purity of waters polluted by domestic sewage. By way of illustration we shall now present Woodywiss' table and give examples of its application.

Table

Assessment of Water Purity by Biotic Index

Bioindicators	Indices	No. of groups present				
		0-1	2-5	6-10	11-15	16 and over
Stone fly larvae present	more than 1 species	-	7	8	9	10
	only 1 species	-	6	7	8	9
May fly larvae present	more than 1 species x)	-	6	7	8	9
	only 1 species	-	5	6	7	8
Caddis fly larvae present	more than 1 species xx)	-	5	6	7	8
	only 1 species xx)	4	4	5	6	7
Asellus present	all the above species absent	3	4	5	6	7

Table (continued)

Bioindicators	Indices	No. of groups present				
		0-1	2-5	6-10	11-15	16 and over
Gammarus present	all the above species absent	2	3	4	5	6
Tubificids or (red) chironomoid larvae present	all the above species absent	1	2	3	4	-
All the above species absent	some species not demanding oxygen may be present, e.g. Eristalis tenax					

x) Excluding Baëtis rodani

xx) Including Baëtis rodani (May fly)

With 2 to 5 hydrobiont "groups" and more than one stone fly species found in the benthos samples taken at the control station, the biotic index is 7. With 2-5 "groups" present in the samples, all of the foregoing organisms absent, but with tubificides or chironomids present, the biotic index is 2, i.e. the water is highly polluted. To expand the geographical range of the Woodywiss system for it to be applicable in assessing the purity of waters polluted by industrial effluents, the equiecological indicator species characteristic of the region in question should be incorporated into the table used to estimate the biotic index.

For example, we have adjusted the Woodywiss system for water indication in Western Siberia.

It is to be borne in mind, however, that the impact of pollution may induce in the indicator species latent changes capable of causing their death. Meanwhile, the indicator organisms may be present in quite sufficient numbers at the time of water purity measurement, thus leading the investigator to wrong conclusions about the water quality (10). In his well-known monograph V. Sladeček (31) lists 33 comments made by the experts with regard to the various water quality bioindication techniques. G.H. Vinberg with co-workers compared the indicator capabilities of different methods applied under identical conditions (4). Unable to dwell on this question at length here, I consider it necessary to stress that all the numerous methods for bioindication of water quality are founded on common morpho-taxonomic and ecological-physiological principles. So there is no need to multiply "national" systems and methods of water quality assessment - it suffices to adapt the more felicitous of them in the regional aspect. In doing so it is rational to effect the method suggested by Pantle and Bukk in the Sladecek's modification (16, 31) as a standard method. For a more detailed discussion of the water quality bioindication techniques with a particular reference to their practical applications, we recommend the following literature (11, 12, 21 and 22).

In conclusion, let us note that the water quality bioindication methods are receiving an ever growing attention in different countries. Thus, the Commission of European Communities brought together on three occasions experts from different countries for them to evaluate water quality in specific water bodies, using their own national methods (30). Scientist from the member countries of the Council for Mutual Economic Assistance meet regularly to discuss bioindication of water quality. The USSR Hydrometeorological Service (13) sponsored recently a National Conference and two USSR-UK and USSR-USA Symposia (4, 8, 17) on the scientific fundamentals of water quality monitoring by hydrobiological indices and on the mathematical models for water quality management (9). An examination of their proceedings leads to the conclusion that at the current stage in the development of science the elaboration of biological methods for water quality analyses is a top priority task because it would take a long time and a great effort to create a quantitative data bank on the functioning of ecosystems (2,3). It remains to add that organisms alone, and not mathematica calculations, can supply reliable information about the biological adequacy of water and the processes that effect it.

It is thus seen that an effective biological monitoring service for water quality assessment should be based on natural systems of water quality bioindication which reflect objectively the laws of nature. Otherwise, as V.I. Lenin wrote: "Human projects disregarding the great laws of nature bring only misfortunes" *)

---

*) V.I. Lenin. Synopsis of correspondence between K. Marx and F. Engels. Moscow, Politizdat, 1959, p 378 (in Russian)

REFERENCES

1. V.A. Abakumov. K istorii kontrolya kachestva vod po gidrobiologicheskim pokazatelyam. - Nauchniye osnovy kontrolya kachestva vod po gidrobiologicheskim pokazatelyam (To history of water quality assessment by hydrobiological indices. - Scientific Principles of Water Quality Assessment by Hydrobiological Indices), Moscow, Gidrometeoizdat, 1981, pp 46-75.

2. L.P. Braginsky. Novaya sistema biomonitoringa vodnoy sredy v SSHA (New system of aqueous medium biomonitoring in the USA). Hydrobiological journal, vol 14, No.1, 1978, pp 77-83.

3. G.G. Vinberg. Problemy i organizatsiya issledovani vnutrennikh vod (Problems and organization of hydrobiological researches in inland waters). Hydrobiological journal, vol. 17, No.1, 1981, pp 3-10.

4. G.G. Vinberg, A.F. Alimov, E.V. Balushkina, V.N. Nikulina, N.P. Finogenova, S.Ya. Tsalolikhin. Opyt primeneniya raznikh sistem biologicheskoy indikatsii zagryaznenlya vod (Experience of application of various water pollution bioindication systems). In: Scientific Principles of Surface Water Quality Assessment by Hydrobiological Indices. Leningrad, Gidrometeoizdat, 1977, pp 124-131.

5. V.I. Zhadin. Biologicheskiye priznaki zagryazneniya vodoyomov i puti ikh izucheniya v Sibiri (Biological features of water bodies pollution and ways of their study in Siberia). In: Matter and Energy Circulation in Lacustrine Water Bodies. Moscow, Publishing House "Nauka", 1967, pp 10-15.

REFERENCES (continued)

6. V.I. Zhadin. Problemy sanitarnoy gidrobiologii vnutrennikh vod (Problems of sanitary hydrobiology of inland waters). In: Sanitary and Engineering Hydrobiology. Moscow-Leningrad, publishing house "Nauka", 1967, pp 5-17.

7. V.N. Zhukinsky, O.P. Oksiyuk, G.N. Oleynik, S.I. Kosheleva. Projekt sistemi komplekснoy otsenki kachestva poverkhnostnikh presnikh vod (Project of system of complex quality assessment of surface fresh waters), Water Resources, No.3, 1978, pp 83-93.

8. Yu.A. Izrael, N.K. Gasilina, V.A. Abakumov. Gidrobiologicheskaya sluzhba nablyudeniy i kontrolya poverkhnostnikh vod v SSSR (Hydrobiological service of surveying and control of surface waters in the USSR). In: Scientific Principles of Surface Water Quality Assessment by Hydrobiological Indices. Leningrad, Gidrometeoizdat, 1981, pp 7-16.

9. In: Mathematical Models for the Optimization of Water Quality Management. Proc. USSR-USA Symp. Kharkov-Rostov-on-Don. Leningrad, vol. 2, part 2, 1979, pp 145-148.(in Russian)

10. E.N. Levitova, M.M. Telitchenko. Primeneniye gistologicheskikh metodov issledovaniya dlya resheniya nekotorykh voprosov sanitarnoy gidrobiologii. Bull. Moscow Soc. Nat. Scientists, dept. biol., vol. 64, No.2, 1959, pp 45-48 (in Russian).

11. A.B. Makrushin. Biologicheski analis kachestva vody (Biological analysis of water quality). Leningrad, AN SSR Press, 1974, p 60.

REFERENCES (continued)

12. A.B. Makrushin. Bibliographic index on:"Biological Analysis of Water Quality" with an attached list of pollution indicator organisms. Leningrad, ZI AN SSR Press, 1974, p 51 (in Russian).

13. In: Scientific Principles of Water Quality Assessment by Hydrobiological Indices. Proc. Nat. Conf. Nov. 1-3, 1978, Leningrad, Gidrometeoizdat, 1981, 207 pp.

14. L.G. Ramensky, I.A. Tsatsenkin, O.N. Chizhikov, N.A. Ankipin. Ekologicheskaya otsenka kormovykh ugodiy po rastitelnomu pokrovu (Ecological assessment of greenlands by plant cover). Moscow, Selkhozgis, 1956, 471 pp.

15. Sladecek V. General biological scheme of water quality. In: Sanitary and Engineering Hydrobiology, Moscow, publishing house "Nauka", 1967, pp 26-31.

16. V. Sladecek, M.M. Telitchenko. Bioindication of water quality. Inf. bull. on water management for CMEA countries, No.2 (32), 1983, pp 20-23.

17. K.M. Tarzvell. Kratkaya istoriya issledovaniy zagryazneniy vod v SSHA (Brief history of water pollution researches in the USA). In: Impact of Pollutants on Hydrobionts and Ecosystems of Water Bodies. Proc. of two USSR-USA Symp., Leningrad, publishing house "Nauka", 1979, pp 17-39 (in Russian).

18. M.M. Telitchenko. In: Self-Purification and Bioindication of Polluted Waters, Moscow, publishing house "Nauka", 1980, pp 5-6.

19. M.M. Telitchenko. Razvitiye i zadachi sanitarnoy gidrobiologii v SSSR (Development and tasks of sanitary hydrobiology in the

REFERENCES (continued)

USSR), Journal of hydrobiology, vol. 18, No. 6, 1982, pp 22-33.

20. M.M. Telitchenko, K.A. Kokin. Sanitarnaya gidrobiologiya (Sanitary hydrobiology), Moscow, MGU Press, 1968, 103 pp.

21. Standardized methods of water quality research (methods of biological water analyses) with appendices; publishing house "III", Moscow, CMEA (COB), 1976, 165 pp.

22. Ausgewählte Methoden der Wasseruntersuchung (Biologische, mikrobiologische und toxikologische Methoden), B.II, Jena, Veb Gustav Fischer Verlag, 1982, 579 S.

23. Bridgeman P.W. The Loge of Modern Physics. London, 1927, 262 pp.

24. Cairns J. and Dicksen K.L. A simple method for the biological assessment of the effects of waste discharges on aquatic bottom dwelling organism. J.Wat. Poll. Contr. Fed., 43, (5), 1971, pp 755-772.

25. Gabriel J. J Vyestrovaci metody v hygiene. Statni zdravotnicke nakladatelstvi, Praha, 1954, 151 S.

26. Goodnight C.J., Whitley L.S. Oligochaetes as indicators of pollution. Proc. "15th Ind. Waste Conf., Pardue Univ. Ext. Ser.", 106, 1961, pp 139-142.

27. Liebmann H. Methodik und Auswertung der biologischen Wassergütekartierung. Münchner Beitrage zur Abwasser-, Fischerei- und Flussbiologie, No.6, 1959, S. 134-156.

28. Margalef R. Perspectives in ecological theory. Chicago-London, The University of Chicago Press, 1968, 118 pp.

29. Pantle R. Biologische Flüssüberwachung. Wasserwirtschaft, 46, 8, 1956, S. 206-209.

30. Persoone G. and De Pauw N. Systems of biological indicators for water quality assessment. - In Biological Aspects of freshwater pollution (Proceedings of the Course held at the Joint Research Centre of the Commission of the European Communities, Ispra, Italy, 5-9 June, 1978. - Published for the Commission of the European Communities by Pergamon Press, 1979, pp 39-75.

31. Sladecek V. System of water quality from the biological point of view. - Archiv für Hydrobiologie, Beiheft 7 (Ergebnisse der Limnologie), S. 1-218.

32. Woodywiss F.S. The biological system of stream classification used by the Trent river Board. - Chemistry and Industry, II, 1964, pp 443-447.

33. Zelinka M., Marvan P. Zur Präzisierung der biologischen Klassifikation der Reinheit fliessender Gewässer. - Arch. Hydrobiol., 57, 3, 1961, S. 389-407.

POLLUTION OF MARINE ECOSYSTEMS

S. A. Patin

It has now become quite obvious that man disturbs the natural ecological equilibrium in the seas and ocean not only through commercial exploitation of marine biological resources, but also by polluting the marine environment. Indeed, most of the pollutants, once they have got out of man's control, somehow find their way into the marine environment, giving rise to local, regional or global pollution. Owing to large-scale circulation and the integrity of the biological structure of the World Ocean, regional anomalies in any of its parts affect, in the final analysis, the adjoining regions and the system as a whole.

This is why the pollution of the seas and oceans has now become a major international concern, as borne out by the materials of numerous scientific forums, joint research programmes, intergovernmental agreements and the activities of many UN working groups and bodies, among them FAO, WHO, UNESCO, etc. In the decisions of the XXIV Session of the UN General Assembly and of the Special UN Conference held in Stockholm in 1972, among priority ecological problems, the mankind presently faces, special emphasis was laid on the pollution of the World Ocean. A special system for monitoring the pollution of the marine environment has been set up and is now operative within the framework of the UN Environment Programme.

The scope of research activities on the problem concerned is unprecedented. Suffice it to say that more than 2000 articles and books dealing with this problem are published annually. Some of the authors think that time is ripe for a new independent science on marine pollution to be set up, which must not only study sea pollution as a new ecological factor for the seas and oceans, but also be engaged in working out efficient methods for its control.

A particularly violent upsurge of research activities was observed in the 1960s which is associated with the nuclear tests in the atmosphere in 1958-1963, when the biosphere was contaminated with the products of nuclear explosions. The results of these researches had a great impact on the world public opinion and furnished a scientific rationale for signing the 1963 Moscow Treaty on banning nuclear tests in the three media. A similar process takes place at present in the field of chemical pllution; the alarming results of investigations into the pollution of the World Ocean urge large-scale national and international efforts for control and prevention of detrimental anthropogenic impacts on the marine environment and biological resources. The difference lies in the fact that the flows of toxic chemicals into the World Ocean cannot be stopped at once and everywhere, as was the case with the halting of nuclear tests.

In the overall ecological research of the World Ocean pollution we can identify two basic trends. One of them is of the biogeochemical nature and is aimed at obtaining information on the sources and inflow pathways of pollutants into the World Ocean, their content in both biotic and abiotic components of the ecosystems, forms of occurrence in sea water, their distribution and migration in the seas and oceans,

6300 8

etc. In a word, this branch of research studies the origin and behaviour of anthropogenic impurities in the World Ocean.

The other trend deals with the study of biological effects and implications of the marine and ocean pollution. Researches of this kind are based on the results of either toxicological experiments with selective species of marine organisms or field observations over the structural and functional characteristics of marine ecosystems in a polluted environment. In either case we obtain information enabling evaluation or prediction of biological implications of man-induced disturbances in the chemical composition of the marine biotopes.

Neither biogeochemical nor ecological toxicologic researches are, of course, an end in themselves, though the knowledge of the character, scope, and biological consequences of pollution are relevant to forming a correct judgement on the potential danger of pollution and ways to control it. These researches can and must directly contribute to the prevention of sea pollution, for instance, by specifying permissible levels for the discharges of noxious substances into the marine environment, by exercising biological control involing biological tests of waste-waters and their individual components, etc.

It is to be emphasized that the trends of research, briefly discussed above, supplement each other and provide an overall picture of the World Ocean pollution. Biogeochemical investigations study the effects of hydrobionts on the distribution, migration and transformations of pollutants in the marine environment, whereas marine ecological toxicology deals with a reverse problem, namely, the effect of these impurities on marine organisms, their populations, communities and the biotic cycle in the ecosystems. Thus, these two trends of research study two aspects of a single process of marine organism interaction with their man-infringed biotopes and constitute in effect, the basis of ecological knowledge without which efficient national and international efforts for protection of seas against pollution would prove impossible.

Quite recently an opinion was current that in view of the grand volume of the World Ocean (namely, $1.4 \cdot 10^9$ km^3 at an average depth of 3,800 m) no concern should be aroused about the purity of its waters, the problem itself falling, in fact, into the solution of a number of local tasks which do not surpass the confines of individual maritime states. Furthermore, it was proposed that seas and oceans by virtue of their great depths may be used for dumping different kinds of wastes, including radioactive ones. Today these concepts have been subject to a radical revision on the basis of abundant factual material amassed by the researchers in many countries of the world.

In analysing the present situation in the pollution of the World Ocean we have to admit, above all, the fact of the ubiquitous radioactive and chemical contamination of the marine environment. Modern sensitive methods of analysis, applied to the samples of sea water and organisms taken practically at any point of the ocean (from the Arctic to the Antarctic), enable us discover numerous traces of man's activities, including man-made radioisotopes (strontium-90, cesium-137,etc.), organochlorine substances (DDT, polychlorbiphenyls, etc.), oil and oil products, heavy metals. Some of these substances (metals, oil) have ever existed in nature and man has simply changed their natural concentration and the form of presence in the marine environment, whereas others (for example, DDT, strontium-90) are endebted for their appearance in nature to man alone.

A composite list and certain characteristics of the most widespread pollutants are given in Table 1. A common and characteristic feature of all these substances is a significant air-borne share of pollutants (up to 80-90%), in their total input into the marine environment, thus indicating the presence of an atmospheric reservoir for each of these. Crude oil is the only exception, its input to the World Ocean is practically independent of the atmospheric transfer. Nonetheless, oil is indisputably one of the most characteristic pollutants for the marine environment, since more than half of its total input, to the hydrosphere is associated with sea transport and shelf oil mining, creating long-living fields of oil pollution in the open sea and ocean. The highest levels of petroleum hydrocarbons are found in inland seas, coastal and shelf zones, estuaries and river deltas, as well as in the sea areas traversed by traditional oil-transportation routes and emergins as centers of oil mining at present and in the future.

The most widespread pollutants in the group of heavy metals are usually mercury, lead, and cadmium. It is these elements (particularly mercury and lead) that on account of their physical properties are emitted into the atmosphere in the course of burning up of all kinds of fossil fuel. Thus, at burning the crushed coal as much as 90% of mercury is converted

Table 1

Most common toxic constituents of large-scale pollution of the World Ocean

Groups and constituents of pollutants	Priority (a)	Degree of biological hazard (b)	Distribution
Radionuclides:			
Strontium-80	1		global
Caesium-137	1		global
Plutonium-238	-		global
Tritium	-		global
Cerium	-		global
Chlororganic toxicants:			
DDT and its metabolites	2	++	global
Polychlorinated biphenyls	2	++	global
Aldrin	2	++	global
Dildrin	2	++	local
Lindane	2	++	local
Metals:			
Methyl-mercury	1	++	global
Cadmium	3	(+)	global
Mercury	4	++	global
Lead	4	(+)	global
Zinc	-	+	local
Copper	-	+	regional
Arsenic	6	(+)	regional
Chromium	-	(+)	local
Iron	-	-	local
Magnanese	-	-	local
Oil and oil products:	5	+	global
Detergents	-	?	regional

NOTE. (a) Priority indices from the viewpoint of involved hazards for man are given in accordance with recommendations of the UN Environment Program (UNEP, 1974).

(b) The degree of biological hazard for marine organisms:
++ great; + significant; (+) little; ? indefinite; - insignificant (GESAMP, 1973).

into the gas phase. Significant quantities of mercury vapours go over into the atmosphere also as a result of the increased degassing of the upper layers of the earth's crust due to land cultivation, open-cast mining of minerals and other kinds of man's activities involving disturbance of the earth's surface.

All the other fairly numerous industrial and agricultural applications of heavy metals (for instance, mercury in the paper and pulp industry, in the chlorine and sodium production; in the production of organomercury fungicides for seed treatment; use of lead in the paint and varnish industry, etc.) happen to be the sources of local or regional pollution.

The forecasts pertaining to changes in the emission of heavy metals into the atmosphere and ocean are unknown. However, if we admit that the discharge of mercury and lead increases in proportion to the quantity of ash in the atmosphere (Izrael, Teverovskii, 1971), then by 2000 the global emission of heavy metals into the atmosphere and ocean will become at least six times more. These figures are believed to be on the lower side, since this estimation fails to take account of the rest of the input pathways of pollution unrelated to the utilization of the energy derived from fossil fuels.

Among the particularly widespread toxic chemicals the group of chlorinated hydrocarbons takes special place which, unlike oil and heavy metals, have no natural analogues. This group primarily comprises pesticides (DDT, aldrin, benzylhexachloride) and polychlorinated biphenyls (PCB), i.e., substances which are enjoying today an extremely wide and diversified application both in industry and agriculture. All of them, are sufficiently persistent and at the same time volatile and pass into the atmosphere as vapours and aerosols with the ensuing falling out onto the land surface and hydrosphere. There is abundant evidence on the presence of organochlorines in marine fauna, in all latitudes from the Artic to the Antarctic.

The hitherto synthetized organochlorines in agricultural use total over 3.5 mln tons, 1.5 mln tons having already found their way into aquatic and terrestrial biogeocoenoses. Some developed countries are known to have either stopped or sharply reduced the production and application of DDT. However, since no sufficiently safe and cheap substitutes for this pesticide are yet available and it continues to be used in a number of countries, the risk of pollution of the marine environment with persistent and toxic organochlorine compounds is as great today as ever before. Particularly alarming is the growing input into the marine environment of polychlorinated biphenyls, the substances with a very wide range of diverse commercial applications. Their toxicity and cumulative buildup in living organisms are close to those of DDT. However, in contrast to pesticides, placing of biphenyls under control, nationally or internationally, proves far more difficult. Suffice it to recall that already today there are more than a hundred industries where these substances are widely used and where no acceptable and ecologically safe substitutes for them are available.

Thus, there is every reason to conclude that today a large-scale (global) field of pollutants in the World Ocean exists. A characteristic feature of this field is the existence of the gradient of increasing concentrations of major pollutants in transition from mid-ocean towards the neritic zone, inland seas and coastal waters. A similar gradient is observed while moving from the seabed towards surface waters. This tendency evolves as a result of different processes and phenomena including the terrigenous input of pollutants into the marine environment, their discharge with river runoff and the localization of different kinds of man's activities causing pollution in coastal areas (navigation, off-shore oil and gas mining, etc.).

There has also been recorded a latitudinal effect, i.e., an overall decline in the pollution level from north to south and the confinement of maximum concentrations of radioactive and chemical impurities to mid-latitudes of the northern hemisphere, where major industrial and urbanized zones on our planet are found. As is known, about 90% of all technogenic substances come into the biosphere precisely in this latitudinal band, i.e., 30-70° N.L.

There have been identified certain microstructural features of pollutant fields in the marine environment, such as the mosaic pattern in the distribution of toxicants in sea water and their localization within the thin surface film at the interface between sea water and the atmosphere. The accumulation of all microimpurities in this film, which happens to be the biotope of neustonic marine communities and is playing an important role in aquatic ecosystems, are hundreds and even thousands of times as high as in the underlying water masses.

A highly important specificity of the overall pattern of pollution of the World Ocean is the overlap (mutual intersection) of the maximum pollution and bioproductivity fields.

It should be, finally, stressed that the flows and levels of major pollutants in the World Ocean are relatively stable.

In contrast to single, but heavy local pollution, for instance, in accidents, when the toxicity, having reached its maximum, gradually diminishes, the global pollution not only fails to decline in intensity over a long period of time, but, with respect to certain ingredients, displays an ascending tendency. This is easy to understand by considering the relative stability in time (or even a tendency for increase) shown by the characteristics of the world industrial production with which the inputs and levels of pollution of hydrospheric waters are directly correlated. Another reason behind the relative stability (or growth) of pollution levels in the marine environment and marine organisms is associated with a continuous geochemical redistribution of toxicants between the land and the sea, as a result of the terrigenous discharge of impurities into sea water.

The main difficulty that is apt to arise in the analysis of the aftermaths due to man-induced changes in the chemical composition of the marine environment originates in the fact that the marine population is liable to respond to the presence of a toxic or any other contaminating agent simulateneously in all life-forms in the sea - from the subcellular to the supra-organismal one and further to the ecosystem level. There arises a highly complex mosaic of direct and indirect effects of the toxic impact against the background of the natural dynamics of biological processes in the sea under the influence of natural factors.

Different classifications of biological and ecological effects and consequences of marine pollutions may be found. In the first approximation it seems practicable to distinguish two groups of ecological-toxicological situations depending on the nature and intensity of the operating factor and its confinement, correspondingly, to the zones of lethal or tolerant doses. The first of such situations involve direct toxic effects produced on individual populations and communities and accompanied by the damage on principal physiological-biochemical systems of the organisms and their subsequent death, elimination of some species and populations or pronounced pathological changes at the level of an organism, population and, occasionally, of the ecosystem as a whole. Very impressive and, occasionally, tragic instances of such situations arising usually as a result of disasters or single discharges of industrial and other wastes are sufficiently well-known and have been repeatedly described in literature. The areas of intensive pollution are, as a rule, localized within limited zones and their consequences do not spread out over vast water areas.

The second group of effects, which are not as apparent and have been much less examined, involves the impact of relatively low pollutant concentrations on marine organisms, communities and ecosystmes in the conditions of chronic contamination. Owing to differences in the resistance level of hydrobionts of various classes, different stages of onthogenesis and physiological state an intricate chain of biological reactions and responses arises in the communities, the integral and most essential manifestations of which appear to be changes affecting the stability and homeostasis of the ecosystems. The specific indices of such variations include the declining diversity of species, disturbed rates and relationship between the intensity of the processes of organic matter bioproduction and destruction, in anomalies affecting the dynamics of dissolved oxygen and in other ecological variations whose description and, particularly, prediction at low chronic pollution levels are very difficult and not always possible to carry out.

The "concealed" nature of such consequences compared to acute intoxication (for instance, large-scale fish death) by no means detracts from their seriousness or significance. Rather on the contrary, taking account of the scope and ubiquity of global pollution, as well as of other aforementioned features of the overall distribution pattern of toxicants (confinement of the increased pollution levels to the ones with maximal biomass and productivity, relative persistence of global toxicant concentrations, etc.), we may assume the existence of large-scale anthropogenic ecological anomalies in the ocean. This aspect has not yet been sufficiently studied by researchers, though its importance for the entire problem of pollution is quite evident.

One of the possible ways in searching for the answer to the above question is a joint analysis and pooling of biogeochemical and toxicological data, i.e., information on the content of the globally occurring pollutants in sea water in various regions and on the experimentally determined minimal concentrations of these substances, which give rise to the appearance of their unfavourable effects on the marine fauna and flora (interference with the photosynthesis and respiration rate, with growth rate, survivability, reproduction, etc.).

Summarized data of this kind are to be found in Table 2 which was compiled drawing upon earlier publications (Patin, 1979; Patin, 1982). It may be easily seen that the actual pollution levels in coastal areas and in inland seas, i.e., where the bulk of living matter in the World Ocean is produced, are always overlapped ranges of minimal effective concentrations causing adverse effects of toxicants on aquatic organisms. Rough estimations indicate that a minimal sustained reduction of the bioproduction rate in the marine ecosystems under obtaining conditions of large-scale pollution amounts to at least 10% of the biomasses and produce that would have been obtained in the absence of the man-made background of toxicants (Patin, 1979). This conclusion should be extended to aquaculture, firstly, because the marine farming is concentrated in the coastal zone which is subject to relatively high pollution and, secondly, because toxicological evidence used in Table 2 is largely based on the results of experiments with aquacultural objects (fish, mussels, crustaceans, algae). Should we extend this conclusion also to the fresh-water aquaculture, then for the present world aquacultural output of about 8 mln tons annually the biomass losses in cultivated hydrobionts due to the pollution of the water bodies would amount to over 800 thou.tons/year, of which more than 200 thou.tons/year would be given by marine organisms.

The overall pattern of distribution and biological effect of particularly widespread toxicants in marine ecosystems can be represented as follows. Pollutants entering the World Ocean are irregularly distributed in it, forming areas of increased pollution levels in ecological zones and biotopes with maximum biomasses and productivity rates (euphotic layer, neritic zone, inland seas, contact zones and estuaries, water-seabed and

Table 2

The lowest biologically effective concentrations and typical levels of certain substances in surface waters of the World Ocean

Substance	Lowest biologically effective concentration, mg/l	Concentration levels, mg/l		
		Oceanic pelagic	Neritic zone	Local pollution zones
Oil and oil products	10^{-2}-10^{1}	10^{-3}-10^{-2}	10^{-2}-10^{-1}	10^{-1}-10^{-2}
Organochloric toxicants	10^{-5}-10^{-3}	10^{-6}-10^{-4}	10^{-4}	-
Detergents	10^{-1}-1	10^{-2}	10^{-3}-1	1-10
Mercury	10^{-4}-10^{-3}	10^{-5}-10^{-4}	10^{-4}-10^{-3}	10^{-3}-10^{-2}
Lead	10^{-2}-10^{-1}	10^{-5}-10^{-3}	10^{-2}-10^{-1}	10^{-1}
Cadmium	10^{-3}-10^{-1}	10^{-5}-10^{-4}	10^{-3}-10^{-2}	10^{-2}
Copper	10^{-3}-10^{-2}	10^{-3}-10^{-2}	10^{-3}-10^{-1}	10^{-1}
Zinc	10^{-2}-10^{-1}	10^{-3}-10^{-1}	10^{-2}-10^{-1}	10^{-1}

water-air interfaces). Under long-term chronic effect of low toxicant concentrations the differences in biological reactions and responses of marine organisms, for which their systematic place is responsible, are manifest not so clearly as in cases of short-term acute pollution. Therefore, a sustained large-scale pollution of seas and oceans at the existing toxicant levels interferes with the vital activity and bioproductivity of simultaneously all principal groups of marine population. Against this background a tendency is observed for higher intensity of toxic and threshold effects with smaller organisms, thus reflecting the metabolic and reproduction specifics in the case of smaller species and forms of hydrobionts.

As a result, the marine biotic components particularly vulnerable to global pollution predominantly comprise small-size organisms, including phytoplankton (by the indices of infringed production properties), microzooplanktonic filtrators and the early ontogenetic stages of necton and benthos population.

The scientific-technological progress which has triggered off the ecological crisis will be indisputably able to find, and is already finding, effective technical solutions for limiting the flow of noxious substances into the environment. However, the search for and large-scale implementation of such solutions, including waste-free technologies, etc., remain to be costly and give no realistic expectations for a significant overall reduction of global pollution of the marine environment in the coming decades. For this reason alone the urgency of ecological and biological researches into the pollution of the marine environment and organisms, being pursued today throughout the world, is bound to become even greater in future. These researches can and should make a scientific contribution to solving numerous practical problems of protecting the purity of marine water bodies.

REFERENCES

Izrael Yu.A., Teverovskii E.M. Possibilities of large-scale use of atomic energy for securing radiation safety of the population. - Atomnaya energiya, 1971, v. 31, N 4, p. 423-425. (In Russian).

Patin S.A. Ecological aspects of global pollution of the marine environment. - Okeanologiya, 1976, v. 16, N 4, p. 621-626. (In Russian).

Patin β.A. The effect of pollution on biological resources and productivity of the ocean. Moscow, Pishchepromizdat Publishers, 1979, p. 303. (In Russian).

GESAMP - IMCO/FAO/WMO/WHO/IAEA/UN Joint Group of Experts on the Scientific Aspects of Marine Pollution. Report of Fifth Session, Vienna, 1973, 87 p.

Patin S.A. Pollution and biological resources of the Oceans. London, Butterworths, 1982, 287 p.

UNEP (United Nations Environment Programme). - Report of the intergovenmental meeting on monitoring. UNEP/IG. 1/4, 1974.

POSSIBLE ADAPTATION OF HYDROBIONTS TO TOXIC POLLUTANTS

L. D. Gapochka

First organisms, i.e. one-celled bacteria and algae, appeared on our planet about 3.5 billion years ago. The long evolution of life which began at that ancient time gave rise to a multitude of living beings. Their number on the Earth is many millions and they astonish not only by their multiplicity, but also by their wonderful diversity varying from micro-organisms to giant whales and sequioas.

During the evolution process the living beings invaded all the major habitats which are very different in their specific conditions. Aquatic habitat (more exactly - warm oceanic waters) was the first one where life originated and spread. Then life pervaded land and air.

Every living organism can exist only in continuous and intimate association with its ambient habitat whose constituents are very diverse and variable. Complexity and variability of the environment compels organisms to adapt themselves and control continuously their vital activities according to such variations. The ability to adjust themselves to the environment is known as adaptation. The adaptive ability is one of the basic properties of life in general since it allows life to exist, organisms to survive and propagate. The organism and the environment in their interaction constitute an integral system a disturbance of which will eventually result in the organism's death.

During the evolution process the living organisms have improved the regulation and adaptation processes and adapted themselves to the ecological factors of the environment which have surrounded them. Various representatives of the plant or animal kingdom occur both in hot springs having a temperature over +90° and in cold waters of the Arctic Ocean, in fresh waters and in salt lakes. Inhabitants of the aquatic environment are called hydrobionts. They populate the World Ocean, various continental water bodies and underground waters. It is possible to give a great number of examples showing adaptation of plants and animals to various environmental factors.

We shall discuss here the adaptation of animals to low temperatures. The subcutaneous tissue layer of marine mammals such as seals and whales which live in cold waters of the Arctic Ocean is distributed over the entire body. The subcutaneous fatty tissue in several species of seals is up to 7-9 cm thick and its total weight accounts for 40-50 per cent of the body weight. The heat insulation of this layer is so high that the snow under seals resting for hours does not melt although the body temperature of the animals is 38°.

Most ecological factors such as temperature, light, wind, precipitation, etc. vary in space and time. However, all the living beings have adapted themselves in the process of long evolution to such variations and created adaptive mechanisms ensuring their normal development in the conditions of changing habitual ecological factors.

Any organism can live in the environment whose conditions only vary within a certain range. The environmental factors, especially abiotic ones, are characterized by minimum and maxi-

6300 a

mum values beyond which the organism is apt to die. Both the total absence or insufficient amount of the factor necessary for a biological system, and an exceeding dose of this factor are equally fatal to the organism. Between maximum and minimum there is an optimal range of the exposure to the factor within which the vital functions are realized in the most active mode and the population is the largest in number. The minimum and maximum values of factors (threshold levels) at which the life of a given species is still possible constitute the lower and upper limits for its tolerance zone, its stability to variations zone, its stability to variations of the factor whose levels rather often go beyond the optimal range. Within the tolerance zone the variations of the factor do not threaten to cause the organisms death.

"It is remarkable that in the process of the biological evolution the nature is able to find a "mean" intensity of the broadly varying environmental factor and to generate the adaptations just to that intensity" (Aleksandrov, 1975)*. The tolerance zone limits are determined by the genetics of species. However, normally the organism never uses all its potential possibilities and operates, therefore, within a narrower zone than it is feasible for that genotype. These narrowed limits may be broadened up to marginal values, which depends largely on the degree of adaptation to the given factor, on the physiological state and development stage of the organism or population, as well as on the influence of other environmental factors.

Beyond the tolerance zone there is the so-called resistance zone, i.e. the zone of lethal concentration exposure.

---

* Aleksandrov V.Ya. Cells, macromolecules and temperature. Leningrad, Nauka Publ., 1975, p. 286.

Thus, in ecological and physiological studies one differentiates between the tolerance of the organism and its resistance to environmental factors. Accordingly, the adaptation to moderate exposure, i.e. the tolerance zone (capacity adaptation), and the adaptation to extreme doses, i.e. the resistance zone (resistance adaptation) are distinguished (Prosser et al., 1967).

Partial or complete reconstitution of the metabolic activities at different levels of the organization occurs within the tolerance zone, while no such normalization is noted within the resistance zone.

The organism's ability for reproduction shows that it possesses a certain combination of features ensuring its survival in one of the variety of existing media, hence demonstrating the organism's suitability to that medium.

Adaptation is intimately associated with such a concept as a stability of biological systems. This stability is usually interpreted as the ability to overcome the environmental changes and return to the initial functional state after some shifts of the homeostasis. The concept of "stability" is generally applicable to the action of individual factors. The stability of the organism to numerous environmental factors creates its total stability system and its total viability. The better the organism has adapted itself to the given factor, the higher is its stability to the factor variations.

The most important stability mechanism for the population is its heterogeneity (polymorphism) that arises from a mutant spectrum present in the population (this spectrum is often called a mutation burden since under the conditions favourable for the population development the presence of such mutants is undesirable). However, when the external conditions deviate from the normal reaction, it is the existence of such mutants that allows the population to survive in the changed conditions. In this case the dominant form either is eliminated from the population or remains at some level and the mutant suitable for the population becomes to be dominant. In other words, a change in the environmental factor leads to the reconstitution of the population towards a more stable form.

Man has greatly changed the nature of our planet. Initially it was hunting and then agriculture, industry, transportation. Thus, new environmental factors have appeared known as anthropogenic and constituting all forms of social activities that change the nature as a habitat for other species or exert an immediate influence upon their lives. The importance of the anthropogenic impact on the entire living world of the Earth increases rapidly since the scale and diversity of forms of the human productive activities are growing. All the organic world faces the problem of adaptation to these new factors, many of which become truly ecological. Among them it is possible to cite hundreds of new synthetic substances entering the aquatic reservoirs or atmosphere.

The living organisms are far from always possessing the mechanisms providing adaptation to current chemical composition of the environment which is rapidly changing qualitatively and quantitatively.

Adaptability to pollutants could be defined as the ability of the organism to tolerate exposure to these substances without pathological effects. Therefore, the main task in studying the adaptation of the organisms or the population to toxic compounds is primarily in the clarification of the adaptability limits for the object under study to a given substance, i.e. to determine the maximum amount of the substance to which a complete adaptation of the organism is possible.

Those chemical compounds and their concentrations to which the organisms adapt quickly are likely to be less dangerous to the organism than substances to which their adaptation develops slowly. However, it is important not only to know the maximum allowable concentrations of some substances for adaptation, but it is necessary to identify the compounds to which no adaptation is possible (e.g. mutagenes).

Different species of hydrobionts which are very close in their systematic position possess different resistance to the toxic factor. Therefore, the presence of toxic substances in the environment results in the preferential growth of the most resistant species and in the suppression of the most sensitive forms. This redistribution of species may cause structural variation within the aquatic community and eventually change the total productivity of an aquatic reservoir. This production aspect alone shows the importance and necessity to study the hydrobiont's adaptation to various pollutants of aquatic reservoirs.

The other aspect of the problem is connected with studying the adaptation mechanisms developed by individual hydrobionts species to the toxic factor since these mechanisms are responsible for different resistance of these species to pollutants.

The adaptation degree of hydrobionts should be taken into consideration in designing measures for control of environmental pollution. As is known, one of such measures is to determine the maximum allowable concentrations (MACs) for certain pollutants; this has already been done for many hundreds of toxic substances. MAC is the substance amount in milligrams contained in one liter of the fishery reservoir causing no evident pathologic changes in the hydrochemical regimen or the vital activities of hydrobionts at various trophic levels. Thus, the MAC for crude oil is equal to about 0.01 mg/l, and for phenol this value is 0.1 mg/l.

If we consider the maximum allowable concentrations from the viewpoint of the organism adaptation to the habitat, then the MAC can be defined as the maximum amount of substance to which a complete adaptation of the organism and its population is possible. This maximum amount can be designated (Stepansky, 1973) as "measure of the biological adaptation limit" (MBAL).

A sufficient number of experimental and natural evidences which suggest a possibility of the hydrobiont adjustment to increased concentrations of pollutants is available in the literature. Thus, populations of the organisms resistant to heavy metals occur in the nature where such metals are contained in increased amounts, e.g. in sites of polymetallic ore outcrops. A number of forms of bacteria and algae resistant to those metals were isolated from aquatic reservoirs with an increased content of copper, nickel, molybdenum and vanadium (Lyalikova, 1959 and others).

Successful adjustment of hydrobionts to toxic compounds depends on a number of points. One of the reasons for different adaptation of organisms resides in different mechanisms underlying the actions of the compounds involved. The greater the specificity of the pollutant's action (selective reaction with one or several metabolites, enzymes or structural proteins), the greater its toxicity and the less number of chances the organism has for a successful adaptation to its action.

Various toxicity of substances and different degree of the adaptation thereto are also ascribed to the degree of the "acquaintance" of living organisms with such compounds since during the process of long evolution all living beings have adjusted themselves and elaborated their relation to the chemical compositon of their ambient media.

Toxicity of elements which abound in the earth crust (e. g. oil) is usually lower than that of elements which rarely or never occur in it (e.g. dispersants used for removal of oil film).

There is a viewpoint that at a population level hydrobionts adjust themselves to exposure to toxic substances entering the aquatic reservoirs only by selection and maintenance of existing resistant species and by elimination of low-resictant portion of the population. This way (selection of such ready resistant forms within the genetically nonuniform, heterogeneous population of algae) is the basic adaptation mechanism for certain blue-green algae.

At the level of ecological systems the heterogeneity manifests itself in diversity of species that provides the so-called nonspecific buffering, i.e. the ability of an ecological system to resist to alternating or damaging impact of the environment. The experiments showed a clear correlation between phenol degradation rate and the species diversity of microcenosis. It was found that initial biocenoses consisting of various embodiments of water thyme, duckweed, mollusca, oligochaetae and microscopic organisms introduced with natural water and specifically unfit to degrade phenol are gradually substituted by biocenoses which are capable for its degradation, and the property to degrade phenol in this case appears as the property of a newly emerged system. This is proved by the fact that on ceasing the introduction of phenol into the microcenoses which are adapted to degrade this toxicant they lose quickly enough their acquired ability. A deadaptation of biocenoses occurs. Therefore, when the toxicant introduction is resumed the microorganisms are no longer able to degrade the toxicant. It took about 50 days to develop new efficient ecological systems.

Therefore, the buffering of the system is determined by its ability for a rapid reconstitution in accordance with changing conditions rather than by its invariability. The wider the species diversity of the system, the higher is the probability of the presence of those species which, having become the main constituents of the reconstituted ecological system, will increase its stability to certain changes in the habitat.

To obtain the effect of adaptation to the toxic action it is necessary for the toxicant to be contained in an amount sufficient to induce an adjusting response, but low enough not to damage the organism.

Small concentrations of toxicants promote the development of specific stability to a certain compound in the organism, population or ecological system, while larger doses can destroy even the nonspecific stability systems. Therefore, adaptation to the toxic or polluting factor is often taken to mean an increase in the living system's adaptability under prolonged exposure to a small amount of the substance or under gradual rise of that amount. The same biological system can cope with considerably higher concentrations of the toxicant when the latter is added gradually as compared with the case when the same toxicant is introduced in a significant quantity at once. Thus, aquarium microcenoses into which phenol was introduced for one year by small increasing doses (from 1 to 10 mg/l) processed rather successfully and quickly the phenol in a concentration of 2388 mg/l. When the toxicant was introduced at a considerably lower dosage (1000 mg/l) at one time the aquarium ecosystem was destroyed (Kamshilov, 1973).

All the above mentioned facts evidence that the adaptation of hydrobionts to the toxic action of a pollutant is essentially feasible, but it depends on a number of factors and primarily on the species and physiological state of the organism, on dosage, time and mode of action of toxic compounds, as well as on environmental factors (e.g. temperature).

The adaptation to toxic action is intimately associated with such concepts as harmfulness or harmlessness of changes under the action of chemicals on the organism or its population. Therefore, it is important to reveal the differences between physiological adjustment response (to the action of harmless concentrations of chemicals) and the compensatory reactions of the emerged pathological process (to the action of harmful concentrations), i.e. to ascertain the region lying between the norm and pathology. To assess the margin between true physiological adaptation and compensation for the pathological process is very difficult. For example, such a region can be established by determining the size of the species population, studying the integrity of the organism as a unified biological system and the unity of the organism and its habitat.

The survival of species and an increase in its population in concrete conditions of existence can be considered as a sign of normal state of the organism or its population which is intimately associated with the ability of species to adjust themselves to the habitat. Conversely, a decrease in its population is the evidence of disturbances in the adaptation process resulting in pathology.

For many years the adjusting reserves have been assessed by placing the organism in extremal physiological conditions (temperature, trophic ones, etc.). Use is made of various other functional or extremal loads of chemical, physiological or biological nature which are usually integral. This makes it possible to reveal a hidden decrease in the adaptive (to functional loads) or compensatory abilities (to extremal loads) of the organism. In other words, the adaptation to toxicants can be accompanied either by preservation of and even increase in the general nonspecific stability of the organism, or by its decrease. The adaptation of the organism is said to be complete if it is accompanied by a full-scale preservation (or increase) of the adaptation abilities in relation to various effects and if the organism or its population maintains the ability to reproduce the posterity which is adequate in every respect. Incomplete (defective) adaptation of the organism imparts a mere semblance of well-being in new conditions since such adaptation is accompanied by a decrease in its general stability.

A study on the completeness of the adaptation of certain blue-green algae to toxicants by the method of functional loads showed that the algae stable to the toxic action of crude oil grew on the nitrogen-free medium better and died off considerably slower than pure culture controls. It points not only to the invariability of the general stability of cells during their adaptation to crude oil, but also to some increase in the adaptation abilities in relation to nonexistent nitrogen. A similar effect was also noted in studies of the completeness of algae adaptation to the toxic action of dispersant. However, the same blue-green algae adapted to sublethal phenol concentration on the nitrogen-free medium died off more rapidly than those in the control.

The problem relating to the limits of true adaptation and temporary compensation has not been solved as yet and requires additional experimental studies. The limits of the organism's abilities during adaptation, in the narrow sense of the word, may be considered exhausted when irreversible damages arise and when the quality of control changes. Although studies for determining limits of usual adjustment responses differing from the harmful action symptoms are not completed, nevertheless a definition (Sanotsky, 1971) is available for the so-called threshold of harmful effect and this definition is apparently suitable for every environment: the threshold of harmful effect of a substance is its minimum concentration the environmental object which causes changes to appear in the organism which are outside the limits of the physiological adaptive reactions, or causes the latent pathology (temporarily compensated) to appear. In other words, the adaptation of hydrobionts to pollutants is only possible at such concentrations of these pollutants which provide or stimulate the organism's metabolism and evoke physiological process responses, i.e. to maximum allowable concentrations, although in these cases certain hydrobionts could become harmful for their consumers.

The organism's adaptation to toxic effects results in an increased resistance to pollutants. Thus, in response to the application of pesticides the races of crop pests emerge which are resistant to them. Wide application of antibiotics has resulted in the emergence of antibiotic resistant strains of pathogens and of the so-called secondary infections induced by fungi which have been previously nonpathogenic. There are also other facts which suggest, on the one hand, a serious risk of losing a great number of species thereby leading to a less varied and poorer genofond of the biosphere, and, on the other hand, an increase in the number of organisms harmful to man.

It should be emphasized that genofond depletion under the action of pollutants proceeds primarily at the expense of long-cycle highly-organized hydrobionts since their species perish before natural selection begins to operate. Species adaptability range varies rather rapidly only in lower-organized short-cycle species (viruses, bacteria, algae, etc.). It is believed that in the distant future a process of gradual disappearance of long lived species and those having a scanty posterity (sturgeons and other fishes) and the prevalence of short-cycle organisms seems to be possible, i.e. a return to the living beings of the initial stages of life on the Earth is likely to occur.

The emergence of the organism's increased resistance to pollutants has a further objectionable consequence: it usually leads to a rise in the content of these substances in hydrobionts. Therefore, certain hydrobionts although they have fully adjusted themselves to toxicants might be dangerous to their consumers including people. Thus, edible mollusca, particularly oysters, in a number of cases contain carcinogenic hydrocarbon benzpyrene. Pollution of all waters of our planet with waste products of nuclear industry, products of radioactive decay as a result of nuclear explosions, as well as with pesticides is increasing. For example, the pesticide DDT was detected in tissues of polar bears, in penguin liver, in whale fat. Certain substances entering the human organism from aquatic ecological systems possess carcinogenic action mentioned above and influence the heredity. The action of many substances on the physiologic functions of the organism is still merely unknown.

Thus, in spite of great limitations and reservations, the answer to the question concerning possible adaptation of hydrobionts to the toxic action is essentially positive. However, the very fact of the adjustment of certain species to the presence of pollutants is far from having only favorable consequences.

REFERENCES

1. Alexandrov V.Ya., Cells, macromolecules and temperature.(1975). Leningrad, Nauka Publishers.

2. Kamshilov M.M., Buffering nature of living system. - Zhurnal Obshchei Biologii. (1973), vol. 34, No. 2.

3. Lyalikova N.N., Physiology and ecology in relation with their role in sulfide ore oxidation, Cand. Sci. Thesis, (1959), Moscow.

4. Sanotsky I.V., Aspects of the theory of the maximum allowable concentration in relation to defining basic concepts of the preventive toxicology. - In: Scientific Fundamentals of Advanced Methods for Hygienic Regulation of Chemicals in the Environment, Moscow.(1971), 5-11.

6. Stepansky G.A., The limits of biological adaptation. - In. Adaptation Under Exposure to Chemicals. (1973). Moscow, vol. 5.

ADVERSE EFFECTS OF ENVIRONMENTAL POLLUTION AND THE TERRESTRIAL FAUNA

A.V. Denisova

Ecosystems possess a broad spectrum of adaptive capabilities. The more complicated the system, the broader the spectrum. Responses of individual biotic components to the random introduction of anthropogenic factors are, however, nonuniform and can result in far-reaching destructive changes in the ecosystem (biogeocenosis). This phenomenon manifests itself most prominently as adverse side effects of heavy metals, industrial wastes, pesticides, and even fertilizers.

Pesticides occupy one of the leading places among the variety of such substances. Having a very broad range of biocidal action and being systematically disseminated on open terrain, they have become globally distributed in all natural zones. At present, the fauna of ecosystems, including terrestrial animals, needs protection from the unfavourable effects of pesticides.

It is important to note that all the principal aspects of toxicologically and hygienically safe application of pesticides are now sufficiently well defined and successfully dealt with. Side effects of pesticides on man and domestic animals are prevented by observing the so-called "waiting time" (period between the last treatment and the harvesting), timely withdrawal of people, cattle, beehives from the affected area, the use of appropriate methods for storing and processing raw materials and food stuffs, observing the prescribed sanitary and other norms and standards.

Other approaches are, however, required to prevent the impact of pesticides on wild animals that are not the object of chemical control. The reason for this lies in the interconnection and interdependence of complex biocenotic relations in nature, different types of pollution (impact and background), etc., rather than in the mechanism of pesticide action on the individual organism. As long as they persist in the environment, pesticides and their metabolites constantly gain entry into the organism of wild animals with the feed, through the respiratory tract and skin. Besides causing direct intoxication they modify the conditions of existence: of the species and quantitative composition of feed organisms, predators, parasites, competitors, for food, etc. Wild animals differ appreciably from the laboratory and domestic species in their sensitivity to pesticides. The significance of all these factors varies for different natural zones (3, 12, 13).

A number of consequences of the penetration of pesticides into living organisms have been well studied. Actuation of certain defence reactions to pesticides has been ascertained for both an individual animal and the popultion as a whole, along with the mobilization of the organism to neutralize and eliminate the toxic agent from tissues. Some authors, however, regard the so-called "habituation" to a pesticide as taking place at the latest stage of pathological processes. To reduce the toxic effect of impact pollution, animals tend to withdraw, temporarily or permanently, from highly contaminated areas, to change their feeding habits and population structure, etc.

Yet very little is known about the specific defence reactions to a particular pesticide. Mainly involved in the population mechanisms regulating the animal numbers and aimed at the preservation of species are the means developed during the preceding evolution.

The response of the biogeocenosis to a particular pesticide can change if other pollutants (both of pesticidal or other type) are present in the environment, so that its effect may be additive, antagonistic, or synergetic. A combination of various pollutants in the environment is now a very common phenomenon. For example, high concentrations of chlorinated hydrocarbons (DDT, and other stable pesticides of this type, as well as polychlorinated biphenyls-PCB) are often recorded concomitantly with equally high levels of heavy metals in the organisms of wild animals (24). This can complicate the side effects since the trace metals and all kinds of industrial wastes are also known to exert a negative influence on the biota.

Mercury, in particular, has an adverse impact on the reproductive function in warm-blooded animals (17). In concentrations equal to or lower than those found in the tissues of wild birds (mallards) it reduces the number of eggs and increases the frequency of egg-laying outside the nest in some industrially developed countries. The fledglings of these birds are more sensitive to threat stimuli, and less responsive to mother's call (20). Soil contamination with arsenic inhibits its microbial activity and causes death of soil-forming earth-worms and other invertabrates (25). The main danger of lead pollution for wild mammals lies in the gradual accumulation of the metal in animal tissues and chronic intoxication. Lead is known to replace calcium in the bones of young animals, which is of great consequence in view of the possible lead transfer through placenta (25). Cadmium can change the growth rate in terrestrial *mammals* (23). Heavy metals accumulation dynamics differs in the tissues of different animal species but, on the whole, their concentrations grow with age (16, 19, 22).

There is a correlation between the levels of mercury, lead, and cadmium in the internal organs and their content in hair, feathers, and claws, which makes it possible to monitor trace metals in animals without dissecting them. The monitoring of these chemical agents is warranted by their entry into the natural ecosystems. Universal occurence of arsenic and mercury in excessive concentrations is a result of industrial and farming activities (15). Elevated lead levels in wild animal tissues are predominantly associated with the development of the motor-road network, while cadmium pollution is mainly a consequence of land cultivation (18). PCB pollution is found in highly industrialized areas and outside them at high levels of accumulation in animal tissues.

Fertilizers applied on a large scale are reported to produce negative effects on terrestrial fauna, though this happens mostly when the regulations of their production, storage, and application are not observed. With an average run-off from agricultural lands, fertilizers containing nitrogen, phosphorus, and potassium (elements involved in the natural turnover) are even capable of improving the feed resources for wild animals in terrestrial ecosystems. This is, however, not always beneficial for phytocenoses (9).

The adverse effects of man-made substances on plants and animals in terrestrial ecosystems can be significantly limited provided that regulations on the application of ferilizers are strictly observed, agricultural and industrial technologies improved, their by-products completely utilized, and all kinds of environmental pollution greatly reduced. The use of pesticides is, however, quite a different matter because they are manufactured to be applied directly on cultivated lands, forests and pastures as inherently toxic substances with the main purporse of destroying the living organisms harmful to the economy and human health.

Fundamental and applied problems raised by the necessity to limit the hamful effects of non-selective pesticides on natural ecosystems are being solved by means of integrated research.

Diverse consequences of the impact pollution of ecosystems by pesticides, in the conditions of the interaction between various factors of natural and anthropogenic origin, are assessed by studying the persistence and distribution of the chemical in different biotic (vegetation cover, invertebrates, birds, mammals, and other animals inhabiting the contaminated territory) and abiotic components, its transfer along animal trophic chains, distribution in organs and tissues. The assessment also includes studies of the behavioural response disorders, functional and morphological abnormalities, changes in the population structure dynamics (numbers, sex and age composition) caused by both the acute (mostly direct) and the chronic (direct and indirect) effects of the pesticide (2).

The direct acute toxic action of pesticides on various taxonomic or ecologic groups of animals in nature has been manifested in their death, reported to acquire in some cases a mass character in many countries following the application of highly toxic seed disinfectants, rodenticides, and insecticides (5). Owing to the measures taken all over the world, cases of mass poisoning of birds and mammals are now much less frequent.

It is important to assess the significance of the acute toxic effect of a pesticide and animal mortality bearing in mind the restorative capabilities of the population and the ecological role of the affected species. Laboratory experiments with Sevin, an insecticide, revealed its high toxicity to springtails (Collembola). The number of these insects in natural conditions was also diminished after exposure to Sevin. However, the population was completely restored a month later because of a short life cycle of springtails and their high resettlement capability. In addition to that, the insecticide totally eliminated their enemies: spiders, predatory mites and others. But on the whole its acute effect on soil organisms is extremely unfavourable, and in natural conditions prolonged. In the tundra, taiga, mixed forest and steppe areas treated with Sevin the numbers of invertebrates (earth-worms, ground beetles, herb story insects, etc.) decreased by 60-90% within one or two months and remained low for several years.

The degree of isolation of the treated territory is of great importance for the pesticidal effect to be manifested. During a trial of sevin as an acaricide on a narrow 200 m wide strip of forest the number of moles (Talpa europaea) was observed to decrease sharply. This stenophagous animal has an ability to move quickly over a territory in search of food (earthworms). Three weeks after treatment the mole population began to be restored rapidly. This can obviously be accounted for by their ability to emigrate from the polluted strip and subsequent immigration from the adjoining unpolluted territories.

The ecological situation on isolated territories is quite different. Sevin was tested on a small plateau of an alpine steppe to control burrow ectoparasites of Mongolian pika (Ochotona pricei), the animal playing the main trophic, topical and landscape-forming role in this biogeocenosis. At the end of the season the numbers of these animals decreased but slightly. However, the reduction continued during the following years, since the isolation of the plateau surrounded by mountains has practically excluded the possibility of the population being replenished by migrants from the untreated territories. Progressive population depression of Mongolian pikas was also maintained by the disturbances in its self-regulation mechanism, because Sevin has gonado- and embryotoxic properties.

Chronic exposure to such compounds is especially dangerous for wild mammals. Sevin, for example, is a low-toxic and, according to laboratory test findings, non-cumulative preparation. But its negative effect on the populations of mammals (bank vole, great gerbil, Mongolian pika) becomes especially pronounced one year after application. In the absence of land cultivation, a more or less stable pesticide (Sevin persists no less than two years under natural conditions) is distributed among practically all the components of terrestrial biogeocenosis, irrespective of the mode of treatment (aerial spraying, application onto the soil surface, treatment of vegetation cover, insertion into burrows). Pesticides contaminate soil, turning it into a source of the secondary pollution of the biota. They penetrate into plants, including the feedstuffs for phytophagous animals, and beasts of prey. This provides the basis for the entire range of direct and indirect changes in the biocenosis.

Having been introduced into a biogeocenosis, Sevin entered muscle tissues of animals, their spleen, liver, lungs, and accumulated in largest amounts in reproductive organs and the embryons (11, 12, 14). Since Sevin specifically affects the mammalian reproductive function (in various rodents, Mongolian pikas, etc.), the number of males and females which did not participate in the reproductive process was observed to increase in the treated areas in many natural zones. There was a simultaneous rise in the occurence of embryon resorbtion, which is a rare phenomenon in rodents under natural conditions. The percentage of young animals having decreased, the population structure changed. Destructive changes on the above-mentioned alpine steppe plateau were observed for a period of several years. Progressive reduction of the pika population resulted in a gradual destruction of empty burrows giving shelter to a number of warm-blooded animals and invertebrates, and their being overgrown with grass. Cessation of animal digging activity interrupted soil transfer onto the surface from its lower layers, resulting in a gradual modification of the phytocenosis.

Side effect of pesticides in nature manifests itself in the secondary intoxication of wild animals, caused by feeding on animals whose organism is polluted with toxic agents. In this respect some rodenticides are especially dangerous for carnivores. This applies in particular to griftor - on the whole a good substitute for zinc phosphide, known in many countries to be harmful to wild animals, including game. Unlike zinc phosphide, gliftor is but slightly toxic for birds in case of either direct or secondary entry into the organism. It is highly toxic for leporids. But pikas, for instance, are known to feed on leaves and stems. Therefore, grain treated with this toxicant presents no danger either for them or for the carnivores that prey on them. At the same time, the presence of large amounts of easily accessible glifter-containing baits in the habitats of granivororous birds is fraught with the risk of their consuming lethal doses of this chemical (6).

Secondary poisoning of animals inhabiting terrestrial ecosystems has been also reported for insecticides, including organophosphorus compunds. Iodofenphos, for example, is poisonous for predatory invertebrates and nestlings of insectivorous birds. The risk of intoxication and total decrease in the numbers of invertebrates, the major feed of these birds during the nesting period, are the most dangerous factors interfering with brood raising.

Another characteristic aspect of pesticidal activity is the effect on animal behaviour. The abnormal behavior of Glifter-affected mammals accounts for their being selectively preyed on by carnivores that are, therefore, running a greater risk of getting intoxicated. Birds affected by dieldrin stop feeding, which causes their death from exhaustion if not from direct poisoning. The general physiological state of nestlings being worsened under the influence of Iodofemphos, the female's behaviour changes. Having to stay in the nest for longer periods to warm the nestlings she almost stops fetching food to them, although behavioural stereotype patterns in the nesting period is quite stable even in the conditions of pesticidal poisoning (7).

Polluted territories scare the birds away. Thus, mass migrations of nesting birds from the forest areas treated with chlorinated hydrocarbons and organophosphorus insecticides have been reported (8). Individual attempts at nesting again a few days after the treatment (e.g., Kwith HCCH) are not very effective. More often, birds returning to the traditional nesting sites avoid settling there if the territory had been treated with HCCH or some other pesticides.

The outcome of birds intoxication in nature depends to a great extent on their ecology patterns, including nest location, the size of individual nesting areas, etc. Treatment of nests of three wheatear species with Iodofenphos in a highland steppe habitat resulted in the death of broods and adult birds only in Oenanthe isabellina that nests in mammal burrows. The powder was readily blown out by the wind from the nests of the two other species (O. oenanthe and O. pleschanka) without any harmful impact on them (4).

Side effects of various chemical classes of pesticides are usually determined by the mode of their direct biological action. Rodenticides are primarily dangerous for carnivorous mammals, insecticides - for predatory invertebrates, etc.

The side effects may be of consequence for other classes of living organisms as well. Some herbicides (triazines, DNOC, etc.) cause significant and long-lasting changes in the composition and component ratio of soil biota. Motor activity of some species of ground beetles is diminshed by arboricide 2,4-D. Chlorinated hydrocarbons (DDT, HCCH and others) can influence the clutch and egg size, hatchability, and other indicators of the bird population state. Many organophosphorus insecticides are also toxic for birds. Carbophos, for example, kills fledglings in forest habitats, although its side effect on the invertebrates is much lower than that of other compounds (1). There exist carbamate insecticides extremely dangerous for mammals, while Sevin causes the shedding of tree fruit ovaries. Chlorophos is dangerous for a number of tree and bush species, etc. That is why in predicting the consequences of pesticide application it is necessary to proceed from the data on its hazard for different classes of living organisms, irrespective of the immediate function of the preparation.

The response of animal populations to a toxicant is predetermined primarily by the mechanism of its action. Neurotoxic compounds must be, therefore, assessed primarily for their possible side effects on the behaviour of animals in natural conditions. Godadotoxic agents have to be characterized by their effects on reproductive processes, embryotoxic agents - by their influence on embryogenesis in more than one generation, etc.

Current (background), as well as recommencing environmental pollution with pesticides, necessitates their monitoring to predict and control the state of the environment for the purpose of nature conservation and the maintenance and enrichment of the Earth's faunal resources. Monitoring involves both the ascertainment of pesticidal pollution and the assessment of the significance of the detected pesticides concentration levels (3, 10).

The combination of practical measures for the prevention of adverse side effects of pesticides on ecosystems and their biotic components should include at least the following:

- use of a pesticide (whenever choice is possible) exerting the least noxious effect on the wildlife;
- use of the lowest pesticide concentration effective in controlling the pest;
- planning and performing pesticide treatments in coopera-

tion with local game and fishing inspection bodies, and environment protection organizations;

- keeping the soil surface free from treated seeds that can be used as feed by wild animals.

These are of couse general measures that by no means exhaust the whole range of problems associated with the regulation of pesticide application. Each particular case requires taking into account the specificity of pesticide action, method of application and potential danger for the components of ecosystems under local natural conditions and the existing pollution level. To diminish the adverse effects of pesticides on the animal kingdom it is expedient to give attention to the renewal of their assortment, reduction of the use of most toxic chemicals, the training of personnel engaged in pesticide treatment, the collection and dissemination of information on individual agents, and the furnishing of commercial preparations with more informative labels containing data on their hazardous effects on the most vulnerable components of biogeocenoses.

REFERENCES

1. Voronova Z.D., Denisova A.V. - Problemy po' otchnogo deystviya sovremenych pestitsidov na zhivotnych prirodnych ecosystem (The Problem of Side Effects of the Currently Produced Pesticides on Animals in Natural Ecosystems): - In "Vliyanie deyatelnosty tcheloveka na prirodnie ecosystemy" (Human Impact on Natural Ecosystems). Sb. nautchnych trudov VNIIPriroda MSH SSSR, M., 1980.
2. Voronova L.D., Denisova A.V. - Metoditcheskie aspecty otsenky opasnosty pestitsidov dlya dykych zhivotnych estestvennych ecosystem (Methodology of the Assessment of Pesticide Hazardous Effects on Animals in Natural Ecosystem). - In "Vliyanie pestitsidov na dykych zhivotnych nazemnych i vodnych ecosystem" (Effects of Pesticides on Wild Animals in Terrestrial and Aquatic Ecosystems). Sb. nautchnych trudov CLOP MSH SSSR, M., 1977.
3. Voronova L.D., Denisova A.V. - Pestitsidy i Prirodnaya Sreda (Pesticides and Environment) - "Priroda i Tchelovek, No. 3, 1981.
4. Voronova L.D., Denisova A.V., Evgenov D.N. - Vliyanie insectitsida iodofenphosa na ptits i bespozvonotchnych gornoy steppy Tuvy (The Effects of Iodofenphos Insecticide on Birds and Invertebrates in the Tuva Mountain Steppe) - In "Vliyanie pestitsidov na dykych zhivotnych nazemnych i vodnych ecosystem" (Effects of Pesticides on Wild Animals in Terrestrial and Aquatic Ecosystems). Sb. nautchnych trudov CLOP MSH SSSR, M., 1977.
5. Voronova L.D., Denisova A.V., Pushkar I.G. - Vliyanie pesti-

tsidov na faunu nazemnych ecosystem (Effects of Pesticides on the Fauna of Terrestrial Ecosystems). VNIITEISH, M., 1981.

6. Voronova L.D., Denisova A.V., Dmitriev R.M., Evgenov D.N., Pereladov S.V. - Vloyanie rodentitsida gliftora na dykych teplokrovnych zhivotnych (Effects of Glifor Rodenticide on Wild Warm-Blooded Animals). - In "Vliyanie pestitsidov na dykych zhivotnych nazemnych n vodnych ecosystem (Effects of Pesticides on Wild Animals in Terrestrial and Aquatic Ecosystems). Sb. nautchnych trudov CLOP MSH SSSR, M., 1977.
7. Voronova L.D., Evgenov D.N., Kuznetsova T.G., Shilova S.A. - Nekotorie tcherty gnezdovogo povedeniya kamenok posle obrabotky gnyozd pestitsidom iodofenphosom (Patterns of Wheater Behaviour after Treatment of Their Nests with Iodofenphos Pesticide) . - Zool. J., v. 57, No. 3, M., 1978.
8. Gvozdak A.A., Pryamoie i otdalyonnoie vliyanie pestitsidov na ptyts (Direct and Long-term Effects of Pesticides on Birds) - Nautchny Centr Biol. Issledovaniy AN SSSR, Pushtchino, 1977.
9. Golovkin A.N., Stok mineralnych udobreniy s selkhozugodiy kak factor, vliyayutshiy na raspredelenie melkych lesnych mlecopitayiushtchych (Run-Off of Mineral Fertilizers from Cultivated Lands as a Factor Affecting Distribution of Small Forest Mammals) - In "Vliyanie deyatelnosty tcheloveka na prirodnie ecosystemy" (Human Impact on Natural Ecosystems). Sb. nautchnych trudov VNIIPriroda MSH SSSR, M., 1980.
10. Baker F.D., Tamasonis C.F., Stone W.B., Bush B. - Levels of PCB and trace metals in waterfolw in New York State- "N.Y. Fish and Game I.", 23, No. 1, 1976.
11. Cumgie P. - Mercury in hair of bobcats and raccoons-

"I. Wild-life Manag.", 39, 2, 1975.

12. Faber R.A., Risebrough R.W., Pratt H.M. - Organochlorines and mercury in common egrets and great blue herons - "Environ. Pollut.", 3, No. 2, 1972.

13. Frieda Yataruch und K. Ondersheka, W. - Belastung freilebender Tiere in Österreich mit Umweltschandstoffen (11) - Gehalt an Bleiund Cadmium in Organen von Feldhasen - "Z. Jagdwiss", 27, No. 3, 1981.

14. Harms U., Drescher H.E., Huschenbeth E. - Further data on heavy metals and organochlorines in marine mammals from German coastal waters. - "Meeresforschung", 26, No. 3,-4, 1977-1978.

15. Heinz G.H. - Methylmercury: reproductive and behavioural effects on three generation of mallard ducks- "J. Wildlife Manag." 43, No. 2, 1979.

16. Irwin L., Mason M.L., Ward A.L. - Lead compounds in Mule Deer and Vegetation along 1-80, Southeastern Wyoming- "Transp. Res. Rec." n 805, 1981.

17. Maegen I.L., Hacher C.S., Schroder G.D. and Weir F.W. - Bioaccumulation of lead and cadmium in the Royal Tern and Sandwich Tern- "Environmental Contamination and Toxicology", 11, 1982.

18. Mitchal R.K. - Studies on acute cadmium intoxication in ovary and uterus of Fanambulus pennanti, Wroughton- "Ind. Health", 19, No. 9, 1981.

19. Ollson M., Kihlstrom J.E., Jensen S., Osberg J. - Cadmium and mercury concentrations in mink (Mustela vison) after exposure to PCBs - "AMBIO", 8, No. 1, 25, 1979.

20. Wickström G. - Arsenic in the ecosystem of man- "Wor-Environ-Health", No. 1, 1972.

effects on three generations of mallard ducks-"J. Wildlife Manag."43, N 2, 1979.

21. Irwin L., Mason M.L., Ward A.L. - Lead compounds in Mule Deer and Vegetation along I-80, Southeastern Wyoming-"Transp. Res. Rec.", n 805, 1981.
22. Maegen I.L., Hacher C.S., Schroder G.D. and Weir F.W. - Bioaccumulation of lead and cadmium in the Royal Tern and Sandwich Tern-"Environmental Contamination and Toxicology", 11, 1982.
23. Mitchal R.K: -Studies on acute cadmium intoxication in ovary and uterus of Fanambulus pennanti, Wroughton-"Ind. Health", 19, N 9, 1981.
24. Ollson M., Kihlstrom J.E., Jensen S., Osberg J. - Cadmium and mercury concentrations in mink (Mustela vison) after exposure to PCBs-"AMBIO", 8, N 1, 25, 1979.
25. Wickström G.-Arsenic in the ecosystem of man-"Work-Environ-Health", N 1, 1979.

ORGANISM-BASED WATER POLLUTION MONITORING

K.S. Burdin

Sound planning of industrial and agricultural development and environmental management implies minimum detrimental effect of man's economic activity on the natural environment. Pollution monitoring services, having pronounced chemical or biological orientation, were set up in many developed countries to appraise the water media state /Israel, 1979/. The former carry out observations over the pollution of the abiotic component (water, bottom sediments, etc.), and the latter are mainly engaged in observations over water organisms. The data available on the excessive pollutant content in the abiotic component usually stimulate laboratory studies of the toxicity of these pollutants for the biota in order to predict the environmental implications of the enhanced pollutant content in water /Filenko, Khobotyev, 1976/. The degree of water pollution can be determined only after the chemical analysis of all the environment components (water, suspension, bottom sediments and biota) is completed. The present paper provides a critical analysis of the literature on the metal-based pollution of water, suspension, bottom sediments, and organisms inhabiting the World Ocean.

Practice has shown that regular analysis of water, soil and suspension samples is costly and labour-consuming. And the data obtained fail to meet the requirements, because disposing but only of a few samples it is impossible to avoid the effect of secondary factors - seasonal factors, water salinity, current, tidal activity, sedimentation rate, organic matter content, etc. The analysis of sea water samples with low metal levels requires large quantities of water.

Metals are classed as those dissolved in water and those adsorbed on suspension particles quite conditionally, according to the mesh sizes used. The mesh sizes applied for the purpose vary greatly and make the comparison of the results a difficult matter.

The metal concentration levels are usually high in water and suspension samples taken in the polluted river deltas. As fresh and saline water mix up, metals may precipitate or become adsorbed on phytoplankton cells. Further on this process may result in the sedimentation of metals adsorbed on inorganic particles. Thus the amount of dissolved metals diminishes due to their adsorption on inorganic particles in fresh water and organic particles (mostly phytoplankton) in saline water.

Little is known so far on the toxicity of various metals and their pathways into marine organisms. Much of the research on environmental pollution with metals is meant to estimate their effect on human health or the eco-system's integrity. From this viewpoint a great disadvantage inherent in the data on metal concentrations in water samples is that they are difficult to be used in predicting hazardous effect on the biota, let alone food chain and human health. There are still other problems pertaining to the collation of data on metal concentrations in water samples from different water areas. Seasons, time of the day, salinity, sampling depth, industrial effluents, hydrological factors (tidal processes, currents) cause discrepancies in the data, and these are the greater, the wider the variations of the above parameters. Therefore the number of samples should be much greater to obtain reliable differences in average values of metal levels.

The researchers interpreting the data obtained from bottom sediments face three major problems. First, the metal concentration reflects not only the ratio of the precipitated metal to the total sedimentation for a given period. Second, the metal concentration in bottom sediments depend on the organic matter content, and this dependence is linear. Attempts were made to take account of this factor and to analyze metal concentration only in relation to the available carbon percentage. Third, even the most accurate and comprehensive analysis of the bottom sediment pollution is of no or little use for assessing the amount of metals available to the biota. Even with a high level of metals in bottom sediments, only part of these will affect the biota found in the upper water layers. This explains why many researchers failed to trace correlation between metal levels in water and the biota with those in bottom sediments.

Criteria for the Selection of Organisms for Monitoring

The criteria for the selection of organisms depend on the premises used in biological monitoring programmes.

Programmes of biological monitoring of marine pollution are drawn up with a view to using such organisms as may be helpful in tackling the following problems:

a) what potentially hazardous substances accumulate in the biota and what the rate of this accumulation is;

b) whether there is any proof of persistant changes in the marine environment.

In the first case the criterion for selection will be the ability of the organisms to accumulate the substances under study and to survive under environmental pollution.

The second criterion presupposes the necessity to measure the rates of pollutant concentrations in organisms as well as to assess. Their seasonal changes and changes in the place they occupy in the food chain.

The system of biological monitoring of the marine environment pollution should comprise organisms sensitive not only to a pollution level and factors contributing to changes in the marine environment, but also to the presence or absence of specific pollutants. As to their specific employment, the marine organisms can be classified into indicator organisms, test organisms and monitor organisms.

Monitor organisms are those which can be used in a quantitative assessment of relative pollution levels of the marine environment by measuring a pollutant's content in their tissues. To use the organisms for monitoring purposes, one should know their biology, most vulnerable life phases, position in a food chain and responses to non-anthropogenic changes in the environment.

The monitor organisms are to meet the following requirements:

1. The accumulation of pollutants to a certain level should not result in the organism's death.

2. Organisms should follow a settled mode of life.

3. The species population in the region studied should be large enough not to diminish after sampling.

4. For long-term observations perennial organisms should be selected.

5. Organisms should be large enough to allow analysis of their tissues.

6. An organism should be tolerant to sea water desalting.

7. Organisms should be easy for sampling and resistant to enough to allow laboratory experiments to be conducted for a certain period.

8. Organisms should possess a high metal concentration factor so that they could be directly analyzed without pre-concentration.

9. Correlation should exist between the metal content in an organism and the average metal concentration level in the ambient water.

10. Within a certain concentration range of pollutants the organism used for monitoring purposes must react unambiguously to the presence of metals so that a correlation between the metal concentration levels in organisms and in the ambient water is observable regardless of the place of sampling or habitat.

Thus, the above requirements should warrant metal accumulation in an organism irrespective of the natural environment. If organisms, living near river deltas, have a definite metal concentration level, then the higher metal content in organisms living upstream may be attributed to either the effect of salinity or the excessive amount of metals. Therefore, one should refrain from final conclusions until the effect of salinity on the metal intake by organisms, selected for monitoring, is established. Apart from hydrological variables (water salinitiy and temperature) other effects, such as seasonal changes, the growth rate of the organism, sex, weight, size and point of sampling should be studied.

Using living organisms for pollution monitoring makes it possible to evaluate the effect of metal pollutants on the biota of the area. The selection of organisms for monitoring is a highly important procedure because of its influence on the subsequent evaluation of metal pollution norms.

An organism may take in metals in three independent ways: directly from solution, with food, and with suspended particles. Naturally, the organisms capable of effective metal intake by all three pathways and concurrently meeting the above requirements are hard to be found. In most publications on the subject, it was assumed a priori that the selected organisms meet all the requirements, and hence no special investigations were carried out.

Some examples of utilizing various species for biological monitoring of the marine environment pollution with metals, are given below.

Shells as Monitor Organisms

Recent years have seen an increase in publications on the use of ark shells for metal monitoring as well as on national and international projects of surveillance over mussels.

The ark shells have a metal concentration factor ranging from 10^3 to 10^6, depending on the organism species and the metal type. Metals enter organisms not only with food and from a solution, but also with inorganic particles.

Despite numerous publications on this problem, little is so far known on the effect of various physiological and ecological factors on the shells' ability to accumulate metals. Some data are available on the effect of the organism's age, weight, size and sex; seasons; place of sampling; water salinity and temperature, and the combined effect of several metals on the general metal intake or in the final metal content in ark shells.

Recent years have seen numcrous publications describing mainly metal levels in shells, collected in various regions of the World Ocean. Their major aim is to identify clean and polluted water areas.

Soviet researchers have collated the levels of Fe, Pb, Zn, Cu, Mn, Cd, Ni and Co in mussels in the Black, Barents and White Seas, and found the highest levels of all metals (except Fe) in mussels of the Black Sea /Burdin et al., 1979/, while in the White Sea these were higher than in the Barents Sea.

The promise offered by mussels as monitors has been confirmed in a number of publications that studied mussels' response to their transplantation from unpolluted areas to polluted ones. The experiment was made in the Triest Gulf /Majori et al., 1978/. Their transplantation to a polluted area resulted in increased metal content in Mytilus galoprovincialis, while a return to clearwater areas led to a slower lowering of the same.

Macroalgae as Monitors

Macroalgae were also proposed for monitoring metal-based pollution. The species used for this purpose most often were Fucus vesiculosus, Fucus serratus and Laminaria digitata, as well as Fucus spiralis, Ascophyllum nodosum, Ulva lactuca to name but a few.

Algae are assumed to accumulate mainly metals dissolved in water, while remaining practically indifferent to metals adsorbed on suspended particles, organic or inorganic. Algae are capable of retaining metals in the thallus tissues for long due to a relatively prolonged period of semi-excretion of metals bound.

The ability of macrophytes to accumulate mainly water-soluble metals and to retain these for a long time in their tissues allowed many researchers to recommend them as monitor organisms. However, it should be borne in mind that it is the natural environment that governs whether metals are dissolved or absorbed on suspended particles. Thus, zinc and cadmium are usually found in a dissolved state, while iron and lead - adsorbed on suspended macroparticles.

Some factors known to affect the metal concentration levels in macroalgae are the species place in a taxonomic group, and the part of thallus sampled.

Inspite of a number of difficulties, which are due to the time difference in water and algae sampling data collation has demonstrated a correlation between concentrations of the dissoluble forms of some metals and their concentration levels in brown algae. Such an approach to the assessment of concentration rates of water soluble metals from metal concentration rates observed in algae is an important part of monitoring programmes provided that account is taken of the secondary effects involved in water sampling and of the environmental factors.

So far researchers have practically ignored the problem of the combined effect exerted by several metals on the accumulation of one of them in the algae.

Recent publications report on the use of benthic algae, falling within different systematic groups, for evaluating the pollutant rate of the marine environment near river deltas, in fiords and in the tidal zones of open-sea areas /Gusarova, Khristoforova, 1978/.

Soviet researchers studied the possibilities of using the widely spread brown algae Cystoseira crinita for monitoring Fe, Mn, Zn, Ni, Cu and Pb pollution of the Black sea /Burdin et al., 1980/. They have found out that the use of a whole layer for this purpose is hardly appropriate since the results obtained, particularly in cases of slight variations of metal concentration levels in water, would fail to be authentic because of the enormous season-related changes in the specific mass of stems and branches. In this case the metal concentration levels in samples reflect the varying contributions of individual elements of the layer, but not changes of metal concentration levels in water. After analyzing the experimental data it was proposed to use for the purpose nOt the whole of the plant, but only a part of it, e.g., the stem of a thallus, 3 to 4 years old.

The analysis of samples provided data whose interpretation was impeded by the lack of information on the rate of accumulation and excretion of metals studied and the ecological and physiological characteristics of monitor organisms used. However, monitors have been mostly used only to assess the rates of their pollution with metals.

A wide application of macrophytes in the programmes of biological monitoring, which include observation, assessment and prediction of the marine environment's pollution with metals, necessitates a detailed study of the algae's ability to accumulate metals depending on their age, individual elements of the layer, season, water temperature and salinity, and on the presence of other metals.

Fish as Monitors

Metals enter fish with food or from a solution and accumulate in its organs and tissues. Metals can be absorbed directly from a solution through the entire surface of the body of the fish, through its gills or via the gastric-intestinal (alimentary) canal after swallowing water. The relative contribution of each pathway has not been determined exactly although metal intake with food seems to be the greatest. According to some researchers this hinges on the fish species and metal types /Polikarpov, 1964/. Fish in river deltas may be affected by higher metal concentration levels than in the off-shore areas. The changes in metal concentrations are a function of changes in the metal concentration factor of phytoplankton, zooplankton and fish, which serve as food for the monitor fish, as well as of the ratio between metals dissolved and those adsorbed on suspended particles. Fish are probably indifferent to the presence of metals adsorbed on suspended inorganic particles. However, they may react to this fraction indirectly by eating filtering organisms which extract metals from this fraction.

The use of fish to monitor other metals has been hindered by numerous problems that are still unresolved.

No publication has so far appeared describing with adequate credibility the relation between metal concentration levels (including mercury) in some fish organs and the average metal content in a water medium. Besides, the data on pelagic fish might well be average indicators of the previous metal impacts fish suffered along its migration route. In some cases, however, the use of fish can be expedient, e.g., the rates of pollution of some very distant areas are to be compared or when it is necessary to outline polluted areas occupied by certain ecosystems.

To sum up, one can say that nowadays the use of fish or its tissues for monitoring metal pollution is premature because no correlation has been as yet established between metal concentration levels in fish organs and those in a water medium. Actually nothing is known on the impacts of such important variables as fish species, age, size or weight, nutrition, water salinity and temperature, season or combined effect of several metals.

Main Conclusions on the use of organisms for pollution monitoring

Inadequate attention to sampling methods results in the depreciation of many data on metal concentration levels in organisms. Therefore, what is required at the present research stage is to undertake an inter-laboratory standardisation of the field sampling methods and of the analytical methods of sample analysis. The study of the biotic and abiotic effects on metal accumulation in organisms, planned for use as monitors, is equally important.

Comparison of data on the effect of such factors as season, species age, weight and size, on the one hand, and the sampling place, water temperature and salinity, and the combined effect of metals, on the other, has demonstrated that natural environment factors can have a pronounced effect on metal accumulation or concentration in organisms. Laboratory studies have proved that water salinity and temperature affect the overall accumulation of metals in marine organisms and their toxicity.

Before attempting observations with the use of monitor organisms, the effects of the natural environment on total metal accumulation should be assessed, since these may vary greatly in their influence on organisms and the comparison of results may cause a researcher to arrive at erroneous conclusions. These difficulties are easily eliminated if the sampling procedure is strictly controlled. This means that sampled monitor organisms are of the same age, size and weight, and sampling is done in the same season and in the same place. Discrepancies due to water salinity and temperature are removed if sampling at a reference station is done concurrently. But even in this case laboratory studies seem advisable in order to ascertain the qualitative and quantitative aspects of the effects which, if not known, hamper the interpretation of the results obtained from monitor organisms.

So far ark shells and macroalgae prove to have been studied best. Among the former Mytilus edulis are used most often as its physiology is better studied and it is widely distributed in moderate temperature waters. The selection of macroalgae with similar features presents difficulty, although some of the green benthos plants (Chlorophycea) can be classed as cosmopolitan, but the fact that they are not perrenial is a constraint for their use. However, only the conjunctive use of mollus and macrophytes for monitoring purposes can provide comprehensive information about the overall metal load on the marine ecosystem.

Chapter VII

CLINICAL TOXICOLOGY (MEDICAL)

Edited by professor B.A.Somov

EARLY DIAGNOSIS, PREVENTION AND TREATMENT OF OCCUPATIONAL SKIN DISEASES CAUSED BY EXPOSURE TO CHEMICALS

B.A. SOMOV

The system of measures state-sponsored in the USSR to improve working conditions beneficially affects the health and prolongs the working life of people. Comprehensive mechanization and automation of production processes, the elimination of arduous manual labour changed in considerable measure the nature of the effects produced on the organisms of working people by factors of the production environment; this helped to considerably reduce the incidence of acute forms of skin diseases. At the same time, the intensive development of the chemical industry and the chemization of various sectors of the national economy, including agriculture, may create preconditions for the development of occupational skin diseases resulting from the immediate contact of the skin not only with widely used in industry low-molecular compounds - the salts of chromium, cobalt, nickel, etc., but also with new substances and compounds - polymers, phenol-formaldehyde and epoxy resins, medicinal preparations, insecticides, etc. The specific features of dermatological morbidity among the populations of Asian, African and Latin American countries are dependent on a whole number of factors. Here, apart from social and economic factors, its structure has been largely influenced of late by industrial factors in areas of new industrial development, oil extraction, etc. In industrialized countries an increasing number of employees suffer from latent hypersensitivity to industrial allergens and preclinical (pre-morbid) states of the organism. Factors conducive to the development of these early manifestations of skin diseases have been studied poorly, which hinders the elaboration of effective preventive measures and methods of therapy.

Assuming special importance for the successful control of occupational skin diseases is their early diagnosis in the initial or even subclinical (pre-morbid) period of their development, when the timely removal of the harmful effects of industrial factors and implementation of other medico-prophylactic measures may result in complete recovery or prevent the further development of a skin disease. In this connection special attention should be given to the correct organization of prophylactic and preliminary screenings and also to the detailed dermatological examination of workers at the early stages in the development of a skin disease with the use of clinico-hygienic and functional methods of early diagnosis, including the staging of cutaneous tests and in vitro immunological reactions.

The dermatologist examining workers must well known their working conditions and work route. He must study in detail the specific production technology concerned and be aware of new chemicals whenever they are being introduced into productionl For this purpose it is necessary to enlist the services of hygienists, sanitary physicians, safety-engineering and other specialists.

When examining dermatological patients at industrial enterprises, special attention must be given not only to the state of the skin but also to the state of the internal organs and the nervous system. The presence of relevant background diseases (foci of chronic infections, functional disorders of the nervous system, helminthiases) may have an important influence on the course and outcome of allergodermatosis of chemical etiology. For the early diagnosis of occupational skin diseases it is very important to familiarize physicians with the main groups of chemicals, since known at present are 350,000 organic substances, several thousand chemical compounds and plants causing allergic and other reactions in the organism of working people.

Description of Chemicals Causing Occupational Dermatoses

All chemicals used in industry may be conditionally subdivided according to their effect on the skin as follows:

1. Substances with a predominantly primary irritative effect on the skin: obligate irritants - concentrated in organic acids and alkalis, the salts of alkaline and heavy metals, substances possessing a dermatovesical action, capable of causing burns and ulceration on contact with the skin.

Facultative primary irritants - cause diseases of the skin in only some of the persons exposed to them. Belonging to them are weak concentrations of inorganic acids and alkalis, the products of processing petroleum, coal, shales.

2. Substances possessing a pre eminently sensitizing effect on the skin: artificial and natural polymers (resins, rubbers, colophony, shellac), medicinal preparations, dyes, the compounds of the metals-chromium, nickel and cobalt.

It should be borne in mind that frequently taking place under industrial conditions may be the combined effects on the skin of primary (obligate) irritants and sensitizers, which leads to the intensification of the latter's sensitizing effect.

Another thing that has to be borne in mind, is that during the working process workers have to endure exposure to the effect of a number of occupational hazards, including unfavourable weather conditions (high temperature and air humidity). A certain effect on the course and outcome of skin diseases is rendered also by mechanical factors, such as friction against moist or rough surfaces, etc.

Some of the chief agents causing at present occupational allergodermatoses (dermatitis, eczema) are at present polymers and polymer-containing compounds. Because of their valuable properties polymers are widely used for the manufacture of plastics, varnishes, glues and enamels. Polymers, the products of polymerization and polycondensation of organic compounds by monomers, are used in most diverse branches of the economy - chemical, radio-engineering and electrical-engineering, rubber, woodworking and furniture making, textile, and many other industries.

The following chemicals are used in the individual industries:

I. Textile Industry

Used here are fibres produced synthetically (dacron, caprone, nylon, etc.); to prevent them from untwisting and from static electricity, artificial yarn threads are covered by various oiling agents, which comprise triethanolamine, a substance possessing a pronounced sensitizing effect.

Also used are various dyes and detergents.

2. Radio Engineering and Electrical Engineering

Used in these industries are phenol-formaldehyde, epoxy and polyester resins, press powders based on them, glass fibres (AG-4), dyes which include compounds of chromium, nickel, cobalt, glues based on phenol-formaldehyde resins, formalin, rubbers and other substances.

3. Rubber Industry

Used are natural and synthetic rubbers, lead, calcium, magnesium oxides; antideteriorants - neozone D; rubber accelerators captax, thiuram; plasticizers - the products of processing oil, coal, etc.; fillers - soots, zinc oxide, copper, kaolin, formaldehyde and epoxy resins; rubber cement.

4. Woodworking Industry

Occupational dermatoses may be caused by varnishes based on shellac resins, colophony, glue, bakelite, phenolformaldehyde, ureaformaldehyde and polyester resins, nitro dyes, nitrolacquers and various solvents (turpentine).

5. Engineering and Metalworking Industries

Occupational dermatoses may be caused by the salts of chromium, nickel, cobalt, by cutting fluids, turpentine, synthetic resins and dyes. In electroplating works occupational diseases of the skin may be caused by the compounds of nickel, chromium, gold and platinum.

6. Printing Industry

Occupational dermatoses may be caused by contact with compounds of metals for the electroplating of formes Used for etching the formes are compounds of chromium - chrompic. The pigments of printing inks containing the compounds of chromium, nickel, cobalt and solvents (turpentine) have a sensitizing effect. Used for the development of black-and-white photo-cine-roentgen films are menthol and hydroquinone, and for developing colour films - diethylparaphenyl formalin sulphate, possessing a pronounced sensitizing effect.

7. Construction Industry

Used here are cement mortars containing the compounds of chromium, nickel, cobalt and unslaked lime, asbestocement, lime. In the production of ferroconcrete slabs an additional sensitizer may be glue containing formalin, phenol-formaldehyde and epoxy resin in combination with liquid glass, oil and nitro dyes with a sharp alkaline reaction, whose pigments contain the compounds of chromium, nickel, cobalt, dye fixers (epoxy and polyester resins), various solvents - turpentine, white spirit, mastics based on various resins.

8. Chemo-Pharmaceutical Industry

The cause of occupational dermatoses in the chemopharmaceutical industry and among medical workers may be the semiproducts and prepared forms of vitamins B_1, B_6, B_{12}, antibiotics (penicillin, streptomycin, chloramphenicol, chlorpromazine hydrochloride and other preparations of the phenothiazine series), PAS, novocain, mercury, furacin, bichloride of mercury, chloramine, rivanol.

9. Agriculture

The cause of the onset of skin diseases among farm machine operators are chemicals (gasoline, kerosine, lubricants, diesel fuel), contact with the metal parts of machines and implements, and also with mineral fertilizers and poisonous chemicals; among those working in animal husbandry: fungi, including yiest fungi, cocci, viruses, bacilli, and also antibiotics and disinfectants; among plant growers and hay-makers: tall buttercup, primrose, poison sumac, parsnip, cow parsnip, tomatoes, citrus plants, figs, celery, garlic, tobacco, meadow and river-bank plants and grasses - sedge, milk-govan, moonseed, and also flowers: narcissus, hyacinths, nasturtium, oleander, arnica, chrysanthemum and other flowers.

In order to substantiate the diagnosis of an occupational disease, the following information is essential:

1. A study of working conditions and the operator's working movements.

2. A detailed description of irritants (according to their effect on the skin) to which the worker is exposed in the process of production.

3. A history of the disease with an indication of the time of its onset when performing duties in contact with chemicals and a documentary confirmation that the disease was not observed before the performance of this particular work. In case of the further development of the disease or its exacerbation an excerpt from the case history of the medical institution at the place of residence or at the place of work must be requested.

4. Treatment of the disease without any contact with the occupational factor.

5. Clinical diagnosis and the location of the process.

6. Functional investigation methods aimed at confirming the occupational nature of the disease (skin tests, <u>in vitro</u> immunological tests, etc.).

7. Inquiries must be made as to whether analogous diseases had occurred in other workers of the same occupation.

It must be stressed that neither of the aforementioned criteria is absolutely valid when taken separately for substantiating the diagnosis, for which their totality only may be sufficient. Special attention should be given to the time and peculiarities in the early manifestations of the skin diseases.

Diagnosis of the Clinical Manifestations of Occupational Skin Diseases Caused by Chemicals

When detecting the pathology the physician describes clinical symptoms: location of rashes, nature of the primary elements (spots, papules, blebs, vesicles, etc.) and secondary elements (erosions, crusts, scaling, cracks, pigmentation, etc.), symmetry, borderlines, etc. Subjective sensations.

The highest incidence of occupational skin diseases of chemical origin among workers of industrial enterprises falls on dermatitis and eczema. Registered much more seldom are toxiderma, ulcerations, lesions of the follicular apparatus, toxic melanoderma and some others.

By their morphological symptoms occupational dermatitis and eczema hardly differ from similar non-occupational diseases.

Dermatitis - is an acute inflammation of the skin appearing at the site of contact with a chemical substance (or other occupational irritant). From the viewpoint of early diagnosis it is necessary to take into account that usually in the early period changes on the skin are only mildly pronounced and are characterized by dryness of the skin of the hands and forearms, its scaling and roughness, the presence of erythematous spots, cracks on the fingers and areas exposed to the greatest contact with the allergen and symptoms of hyperkeratosis. Early changes on the skin precede the appearance of occupational dermatosis. Characteristic of this occupational skin disease is the affection of open areas (hands, forearms, the face).

Dermatitis is subdivided into contact (non-allergic) and allergic (eczematous) dermatitis.

Contact non-allergic dermatitis appears on the site exposed to an irritant and has no tendency to spread to the periphery of the affected area. Termination of exposure results in recovery, usually without relapses. Contact non-allergic dermatitis appears on the skin with unchanging reactivity, and the response inflammatory reaction corresponds to the strength of the irritant.

Not infrequently occupational dermatitis is accompanied with the development of hypersensitivity to industrial irritants (allergic occupational dermatitis) and should be regarded as the early or transitional stage to eczema.

Occupational allergic dermatitis is a skin disease of allergic origin based on hypersensitivity to production allergens; however, since this disease is an early stage of eczema, these patients sensitivity is much less pronounced. Occupational allergic dermatitis is caused most frequently by the salts of chromium, nickel, cobalt, polymers, formaline, antibiotics and a number of other substances.

As a rule, occupational allergic dermatitis develops at the place of the skin contact with the chemicals - on the back of the hands, forearms, on the face, etc. Observed in the foci of dermatitis are erythema, nodular and vesicular rashes of various intensity. Primary elements appear also outside the area of direct exposure to the allergen. Upon the termination of the worker's exposure to the allergen the symptoms of allergic occupational dermatitis rapidly disappear. In a number of patients, particularly during lasting exposure to occupational allergens, allergic dermatitis undergoes transformation into eczema (occupational). Occupational allergic dermatitis must be differentiated from contact dermatitis and occupational eczema. It differs from contact dermatitis in that it is caused by the effect of chemicals possessing the properties of allergens and not of primary irritants (acids, alkalis, etc.). Allergic skin tests in patients with allergic dermatitis are positive in the majority of cases. Differential diagnosis from eczema is carried out on the basis of clinical allergic and immunological examinations.

Occupational eczema clinical symptoms are the same as of true eczema. The distinctive features are the primary location of the eczematous process on the open areas of skin - hands, forearms, face, neck, more seldom on the feet and shins. Characteristic of occupational eczema is that the disease is caused by repeated exposure to an industrial allergen.

Inflammatory symptoms usually abate when exposure to the irritant is diminished (during days off or vacation) and reappear with the resumption of work.

In distinction from dermatitis, characteristic of eczema is a lasting course with relapses and exacerbations. Termination of exposure to the irritant not always ensures recovery. When work involving exposure to chemical irritants is continued, a transition from monovalent to polyvalent sensitization is observed, and not only to industrial, but also to household irritants.

Occupational toxicoderma is characterized by an eruption on the skin of erythematous, erythematous-vesicular and erythematous-bullous or urticarial elements, frequently situated on an edematous foundation. Occupational toxicoderma is caused by chemicals used in industry, by medicinal preparations, mineral fertilizers, insecticides and a number of other agents.

The disease develops acutely, the intensity of the inflammatory reaction usually does not correspond to the strength of the irritant. The inflammatory process abates soon after the termination of contact with the causative chemical.

Occupational ulcerations (anabrosis) develop in workers handling salts, alkalis, in workers involved with the salts of alkaline metals, calcium carbide, cyanide compounds, sodium nitrite, compounds of chromium, nickel and others. Anabrosis appears on the hands, forearms, the upper surface of the foot, on the shins (at the site of micro-injuries). Usually superficial tiny ulcers ("birdseyes") appear, sometimes covered by bloody crusts with infiltrated raised edges. When chromic anhydride is involved, in addition to multiple ulcers on the skin, ulceration of the mucous membrane is possible, followed by perforation of the cartilage of the nasal septum. During healing atrophic scars are formed. Exposure to petroleum and its products may be followed by the development of circumscribed hyperkeratoses and photodermatoses.

Contemporary Methods of Diagnosing Occupational Skin Diseases

The methods of allergological testing and laboratory examinations are important for substantiating the diagnosis of an occupational skin disease. For determining hypersensitivity to chemical irritants in the dermatologist's daily routine the method of drop and compress skin tests is of the greatest importance. Of diagnostic significance is an increase of the eosinophil count in the blood of more than 3-4 per cent, the presence of basophilic leukocyte degranulation, agglomeration of leukocytes and erythrocytes, mast cell destruction, the staging of other *in vitro* immunological tests.

Treatment

The treatment of occupational skin diseases of chemical etiology follows the general principles practised in dermatology. The most important condition for successful therapy is the fullest possible removal of the factors causing the development of allergy. It is important to terminate contact not only with production but also with household irritants, particularly substances with a sensitizing effect. The treatment of occupational dermatosis patients should include general hyposensitizing therapy and remedies aimed at improving the patient's general status. Of great importance in the treatment of occupational allergic dermatoses is a rational external therapy.

It is advisable to use preparations of calcium, sodium thiosulphate, autohemotherapy, etc. Allergic dermatitis and eczema patients are prescribed antihistamine preparations: chloropyramine, promethazine hydrochloride (Phenergan), diphenylhydramine hydrochloride, diazoline. Also recommended is histaglobulin therapy with 5-injection courses; several courses (5-6) are given over one-month intervals. The histaglobulin is injected subcutaneously into the external surface of the shoulder, the first injection is 1 ml, followed by four 2 ml injections over 4-day intervals. Vitamin therapy is indicated: vitamins A, B_1, B_6, E, C, folic acid, nicotinic acid, calcium pantothenate. Prescribed for sleep disorders are the preparations of valerian, bromides, glutethimide, pentobarbital, barbital sodium and others. Prescribed according to indications are diazepam, chlordiazepoxide hydrochloride, trioxazin, meprobamate.

The diet should exclude extractives, spicy and salty dishes, and include a sufficient quantity of vegetables and fruit. The intake of chlorides and hydrocarbons with the food should be restricted.

In case of coexistent "background" diseases (focal infections, diseases of the gastrointestinal tract, helminthiasis, disorders of the nervous and endocrine systems, mycoses of the feet) appropriate therapy should be given. Treatment with short courses of steroid hormones in mild doses (15-20 mg of prednisolone daily) is indicated for severe and persistently relapsing processes only.

External therapy is individualized depending on the clinical picture, the stage of the process, etc., and is conducted according to general dermatological principles. The antiinflammatory remedies include: lead water and 2% boric acid lotion, 0.25% silver nitrate lotion, zinc-in-water suspensions, then creams, pastes and ointments containing ACD, naphthaline, tar, sulfur. Ointments and creams are used containing corticosteroids: prednisolone ointment, flumethasone pivate dexamethasone cream, fluorocort and the like. In most patients these preparations alleviate the acute inflammatory symptoms.

In case of complications caused by pyococcal infection it is advisable to prescribe corticosteroid ointments with antibiotics and other antimicrobial preparations: oxycort, fluicinolone acetonide, flumethasone pivate, hioxysone, and others; when indicated, oxytetramycin ointment may be prescribed for pyoderma foci. In patients with occupational allergic dermatoses accompanied with non-occupational and occupational diseases of the internal organs, the dermatosis frequently takes a torpid course which necessitates the administration of a number of effective therapies.

Following clinical recovery of patients with occupational allergic dermatoses measures should be taken for their proper employment, and suitable occupations should be recommended. As a rule, such patients should be transferred to jobs excluding exposure to sensitizing skin irritants. During the remission period health resort treatment at Sochi-Matsesta with the prescription of hydrogen sulphate baths is of benefit.

In cases where a permanent transfer to another job involves considerable loss of skill ratings, the patient is referred to a medical labour examination board for determining the group of incapacity due to occupational disease.

Prophylaxis

The prevention of occupational dermatites of chemical etiology involves a number of technological, sanitary-engineering, sanitary-hygienic measures, as well as measures of personal protection (special clothing, protective creams, pastes and ointments, detergents).

Taking care of the skin before work, during work and after work is of great importance for the prevention of occupational dermatoses.

The skin may be protected against the effect of various chemicals by different kinds of special clothing (gloves and mittens, special foot-wear, gowns and aprons). In order to increase the strength and resistance to different unfavourable effects the fabrics used for manufacturing special clothing are appropriately impregnated with special compounds or covered by a film coating entirely.

Protective pastes and creams also play a certain role in the prevention of skin diseases of chemical etiology. Such protective ointments and pastes are subdivided into hydrophobic and hydrophilic, according to their action.

Hydrophilic ointments and pastes contain substances readily wettable and soluble in water. They protect the skin against fats, oils, petroleum products, solvents, hydrocarbons, for handling such substances are the protective pastes of the IER-1 and "biological glove" type.

Hydrophobic ointments and pastes include ingredients which are not wettable by water, nor soluble in it (water-repellants). They protect the skin against water, coolant emulsions, aqueous solutions of acids, alkalis, salts and other substances. Most frequently used for protection against these solutions is silicon cream.

All protective ointments and pastes are usually applied to the skin twice (before starting work and after the lunch break) and are twice washed off (before lunch and after work).

The DNS-AK detergent, manufactured by the Shebekino chemical enterprise, is the best means of removing industrial pollutants from the skin.

When handling poisonous chemicals and mineral fertilizers the best protective measures include careful observance of safety-engineering rules, of instructions for their storage. Only persons who have passed a medical examination are admitted to the handling of these substances. Medical examinations are held periodically once every six months. Organophosphorous compounds are rendered harmless on the skin with a 5 per cent ammonia spirits solution and are thoroughly washed off with water; the eyes should be washed with a 2 per cent sodium bicarbonate solution. All handlers of poisonous chemicals must be instructed in the use of "G" and "A" brand cartriges, silicon cream, must know the rules of industrial and personal hygiene and the preventive treatment of minor injuries.

The entire range of medicoprophylactic measures towards controlling occupational dermatoses should be implemented under the guidance and supervision of specialized occupational dermatological rooms attached to the regional dermatological dispensaries, in touch with the sanitary-epidemiological stations, the labour-protection and safety-engineering services and trade-union organizations of industrial enterprises.

Of great importance for the prevention of dermatoses is the organization of preliminary and periodical screenings of workers. Persons who had once had eczema, bronchial asthma, allergic dermatitis, toxiderma, uricaria (hives), neurodermatitis, prurigo, allergic rhinitis, the serum sickness, Quincke's edema and other allergic diseases must not be admitted to jobs involving the handling of chemical irritants. Periodical screenings should be conducted according to established schedules, followed by an analysis of their results, which should be used in the practical activities of the respective production units.

Of great importance for successful control of occupational skin diseases are regular medical check-ups of detected patients with their subsequent rational treatment and job placement.

CURRENT CLINICAL PROBLEMS OF CHRONIC OCCUPATIONAL INTOXICATIONS

A. M. Monayenkova

Chemical substances with diverse structures and physicochemical properties are being increasingly used in the national economy. Under industrial conditions toxic substances enter the human organism through the respiratory ways and the skin as well as via the gastrointestinal tract.

Upon the entry of gases, fumes and aerosols of toxic substances into the lungs they are resorbed in the blood. Following their resorption in the blood and distribution in the organs, the poisons undergo transformations, or biotransformations, and then deposition. Nearly all inorganic poisons, as well as many organic substances, are retained in the body for a long time, accumulating in different tissues. Metals are accumulated mainly in the tissues which contain them as trace elements, and also in the organs with intensive metabolism (liver, kidneys, endocrine glands). Thus, the predominant deposition of lead, beryllium, uranium in bone tissue is closely associated with their ability to form stable, poorly soluble compounds with phosphorus and with their accumulation in bone tissue in the form of phosphates.

The transformation of exogenous substances (xenobiotics) in the body takes place mainly by oxidation and reduction of the ititial substances. Oxidation, as a rule, results in the decrease of the toxic properties of xenobiotics. The oxidation products of some organic substances however may be more toxic than the initial substances themselves. Thus, many organophosphorous insecticides undergo oxidation in the body with the formation of more toxic metabolites.

The toxic substances that have entered the body are eliminated via differents paths - lungs, kidneys, gastrointestinal tract, skin. Volatile substances (benzene, toluene, acetone, chloroform) or volatile metabolites formed by the biotransformation of poisons are exhaled with air via the lungs. Poisons resorbed and circulating in the blood, as well as their metabolites, are eliminated through the kidneys. A number of toxic substances (mercury, arsenic) are excreted through the sweat glands of the skin as well as by the salivary glands. Many poisons and their metabolites forming in the liver are excreted in bile into the intestine.

The structure of toxic substances, their physicochemical properties responsible for the poisons' behaviour in the body, their circulation and elimination, determine also the basic manifestations of their action on the organism.

Depending on their properties and exposure conditions (concentration, duration), toxic substances may cause acute and chronic intoxications.

Acute occupational poisoning occurs suddenly, following a single exposure (lasting not longer than one working shift) to a relatively high concentration of chemicals contained in the air of the working zone.

Chronic occupational intoxication arises as a result of lasting and regular exposure to small concentrations of toxic substances. It should be noted that for many industrial poisons (for example, lead, manganese, metallic mercury, insoluble compounds of beryllium and other metals) only chronic intoxications can practically develop.

Improved working conditions in the leading industries have resulted in a considerable drop both in the incidence and severity of occupational intoxications. Lower concentrations of chemicals at industrial enterprises have brought about nearly complete elimination of acute cases of occupational poisoning and severe forms of chronic intoxication. Typical forms both of acute and chronic intoxications characteristic of the action of toxic substances' high concentrations either completely disappeared or became rare. Urgent at present are investigations into the long-term effects of relatively low concentrations of toxic substances.

Industrial poisons, by exerting a toxic effect on the organism, may cause any of the known pathological processes - inflammations, dystrophic changes, allergic states, fibrous changes in organs, damage to the hereditary apparatus at cellular level, disorders of embryogenesis, the development of tumoral processes, etc.

Moreover, each toxic substance may produce a combination of effects characteristic of the given poison.

Depending on the character of poisonous effects and the system of the organism mostly affected, poisons may be united into the following groups: (1) irritative substances; (2) neurotropic poisons; (3) hepatotropic agents; (4) blood poisons; (5) renal poisons.

This rather tentative division according to the systemic principle does not rule out the polytropic character of toxic effects.

Based on the systemic approach to the effects of chemicals several groups may be singled out among the occupational diseases of chemical origin:

(1) Occupational diseases chiefly affecting the respiratory organs.

(2) Occupational diseases chiefly affecting the blood system.

(3) Occupational diseases of the hepatobiliary system.

(4) Occupational diseases chiefly affecting the nervous system.

(5) Occupational diseases of the kidneys and urinary tract.

Toxicochemical lesions of the respiratory organs are caused by inhaling toxic substances with an irritative effect. They are chlorine and its compounds, compounds of sulfur, nitrogen, fluorine, chromium, carbonyl compounds of metals, soluble compounds of beryllium. In acute intoxication the severity of the lesion of the respiratory ways will depend on the water-solubility of the poison. Toxic substances readily soluble in water (chlorine, sulfur dioxide, ammonia) predominantly affect the mucosa of the upper respiratory ways, the trachea and bronchi. Their effect supervenes without any latent period. Substances that are poorly soluble in water (nitric oxides, phosgene) predominantly affect the deep portions of the respiratory tract. The first clinical symptoms develop, as a rule, after a latent period of various duration. The following clinical symptoms may develop upon acute intoxication:

1. Acute lesions of the upper respiratory ways - acute toxic laryngopharyngotracheitis.

2. Acute toxic bronchitis characterized by diffuse lesions of large and medium-calibre bronchi.

3. Acute toxic bronchiolitis characterized by lesions of small bronchi and bronchioli.

4. Acute toxic pulmonary edema.

5. Acute toxic pneumonia.

A special feature of toxic bronchitis is a rather deep affection of the bronchial tree with the development not only of endobronchitis, but also of peribronchitis, which induces an early occurrence of pneumosclerosis. The associate infection considerably aggravates the course of the process, with a rather frequent result that even after a single intoxication with the development of bronchitis, pulmonary edema, bronchiolitis or pneumonia the disease assumes a chronic course. Chronic lesions of the respiratory organs may develop as a result of lasting exposure to comparatively low concentrations of irritative substances.

Some substances belonging to the group of irritants may manifest a special effect peculiar to them alone. This is true of the compounds of chromium, fluorine, etc. Chromium compounds have sensitizing and carcinogenic effects. Among workers exposed to chromium compounds there are cases of bronchial asthma, allergic dermatites and cancer of the upper respiratory ways and of the lungs.

Exposure to fluorine compounds may result in the development of chronic intoxication known as fluorisis, whereby specific changes develop in the locomotor system in the form of periostal induration in the long tubular bones.

According to their main pathogenetic mechanisms and clinical manifestations, lesions of the blood system under the action of chemical substances may be divided into 4 groups.

1) Affection of hemopoiesis. The main pathogenetic factor in toxic affection of hemopoiesis is depression of proliferation of differentiated blood cells. The toxicants which may cause depression of hemopoiesis include benzene, chlorobenzene, hexamethylene diamine, hexachlorocyclohexane, styrene and other substances.

The clinical picture of intoxication by substances capable of depressing hemopoiesis combines hematological symptoms with disorders in different organs and systems in accordance with the typical effect of the substance concerned.

When the clinical picture is dominated by the anemic syndrome, symptoms typical of many types of anemia are predominant.

When depression of thrombocytopoiesis is prevalent, various manifestations of the hemorrhagic syndrome may develop.

2) Disorders of the synthesis of porphyrins and heme (enzymatic effect). Disorders of porphyrin metabolism are observed during intoxication with benzene, carbon dioxide, acrylates and phosphorus. However, lead causes the most pronounced disorders of porphyrin and heme synthesis, for under its effect they become the primary, determining pathogenetic mechanism of the affection and intoxication. At the earliest stage lead affects the activity of dehydratase of delta-aminolevulenic acid (D-ALA) - an enzyme regulating the initial stages of heme synthesis in the erythrocytes. A decrease in its activity is the earliest and highly sensitive indicator of exposure to lead.

An increase in the content of the metabolites of porphyrin metabolism, delta-aminolevulinic acid and coproporphyrin in the urine, and of protoporphyrin of the erythrocytes in the blood are among the early, reliable and specific indicators of lead intoxication. Anemia in saturnism refers to the group of hypochromic hypersideremic ("sideroachrestic") anemias.

3) Changes in blood pigmentation. The group of blood poisons forming pathological pigments comprises aromatic amido- and nitro-compounds of the benzene series, some medicinal agents whose molecule contains amido/$-NH_2-$/ or nitro/$-NO_2$/ groups, patassium ferricyanide and also carbon monoxide.

Under the toxic effect of aromatic amido- and nitro-compounds hemoglobin is oxidized into pathologic pigments - methemoglobin (MtHb) and sulfhemoglobin (SfHb) which are unable to combine with oxygen thus resulting in the development of hypoxia and cyanosis. The action of methemoglobin-forming agents leads to the appearance of degeneratively altered erythrocytes containing pathological inclusions such as Heinz bodies. The presence of Heinz bodies is responsible for increased destruction of erythrocytes and the development of hemolysis.

The clinical picture of acute intoxication and its severity are determined by the level of MtHb accumulation and resultant hypoxemia.

In chronic intoxication with methemoglobin-forming agents the changes in the blood are manifested as mild anemia of a regenerative character accompanied, as a rule, with compensatory reticulocytosis.

In addition to changes in the blood, the clinical picture of chronic intoxication reveals a number of characteristic syndromes: lesions of the liver, nervous system, eyes and urinary tract. Here, severity of one or another syndrome and peculiarities of the clinical course of intoxication depend on the

the chemical structure of the poison concerned and the nature of the group comprised in the benzene nucleus. Thus, dinitrobenzene mostly affects the blood, trinitrotoluene causes the development of cataract and toxic hepatitis, while binuclear amido compounds affect the urinary tract.

Carboxyhemoglobinemia. Carbon monoxide (CO), when reaching the blood, is absorbed by erythrocytes where it interacts with hemoglobin iron, forming a stable compound - carboxyhemoglobin (HbCO). The presence of HbCO slows down oxyhemoglobin dissociation due to which oxygen deficiency develops. Moreover, CO affects biochemical tissue systems containing iron - myoglobin, cytochrome, cytochrome oxidase, peroxidase and catalase. Simultaneously disorders of porphyrin metabolism take place, indicating the possibility of a direct action by CO on the enzyme systems involved in the biosynthesis of porphyrins.

Chronic intoxication may be due to repeated acute short-term exposures or lasting exposure to low CO concentrations. Most characteristic of chronic exposure are functional disorders of the central nervous system manifested in vegetative dysfunction and the angiodystonic syndrome with a tendency towards angiospasms. Of diagnostic significance is an increased content of non-hemoglobin iron in the blood plasma which has a higher affinity with carbon monoxide than hemoglobin iron, and changes in porphyrin metabolism (increased excretion of delta-aminolevulinic acid and coproporphyrin in the urine). The blood content of carboxyhemoglobin is slightly above the physiological norm (10% and more, the norm being up to 5%).

4. Hemolytic action. Hydrogen arsenide (AsH_3), phenylhydrazine - C_6H_5-$NHNH_2$, toluyene diamine $C_6H_3CH_3/NH_2/_2$ and other compounds cause acute intravascular hemolysis and such substances as amido- and nitro-compounds of benzene may cause chronic compensated hemolysis due to the shortening of the life cycle of erythrocytes.

III. Occupational diseases of the hepatobiliary system arise under the effect of hepatotropic poisons which include: chlorinated hydrocarbons (chloroform - $CHCl_3$, methyl chloride - CH_3Cl, methylene chloride - CH_3Cl_2, carbon tetrachloride CCl_4, dichlorethane - $CH_2ClCH_2Cl_2$, trichloreothylene - $CHCl = CCl_2$), nitro compounds of benzene and its homologues, styrene, trinitrotoluene, compounds of arsenic, phosphorus, phosphorous and organochlorous pesticides, chlorinated naphthalines, etc. Also possible is the development of toxico-allergic or allergic hepatitis upon exposure to substances with a sensitizing effect (ursol, antibiotics, toluylene diisocyanate, etc.).

Of decisive importance in the pathogenesis of toxic damage to the liver is the direct chemical effect on the liver cell, namely its endoplasmic reticulum and the membranes of the endoplasmic reticulum of the hepatocytes.

By their action mechanism on the liver chemicals may be divided into hepatotoxic, toxicoallergic and those affecting metabolic processes; and by the nature of the damage inflicted on the liver - into cytotoxic, cholestatic and mixed. Under the existing classifications of chronic liver diseases toxic hepatitis stands for its clinical morphological features and course closer to chronic persisting hepatitis and the so-called "non-specific" (reactive) hepatitis.

According to the course they take, occupational liver diseases may be acute and chronic. Chronic toxicochemical hepatitis is a benignly proceeding lasting disease, usually without a tendency to progress. Hepatitis aggravated by disordered contractile capacity of the biliary ducts takes, as a rule, a long course.

Characteristic of chronic toxic hepatitis is the gradual development of the disease, beginning with dyspeptic complaints shortly accompanied with the pain syndrome due to the presence of dyskinesia of the biliary tract. The earliest indication that the liver is affected by toxic substances is the increased activity of enzymes organospecific to the liver: fructose monophosphate and aldolase (F-1-PA), urocaninase, ornithine carbamoyltransferase (OCT), alanine aminotransferase (ALT), lactate dehydrogenase (LDH_5). The earliest sign of functional liver cell insufficiency is the disruption of the cell excretory capacity as manifested in the retarded excretion from the liver of radioactive Bengal-rose stain labelled with ^{131}I.

<u>Chemicals affecting the urinary system</u> may be divided into two groups. The first group includes compounds which affect predominantly the renal parenchyma and cause so-called toxic nephropathies. They are heavy metals and their compounds (cadmium, bismuth, lead, mercury, etc.), compounds of arsenic, organic solvents (carbon tetrachloride, dichlorethane, ethylene glycol, etc.), various poisonous chemicals (organomercurial, organochloric and organofluoric compounds), beta-naphtol and others.

Two basic pathogenetic mechanisms of toxic renal affections are singled out. The first one relates to a direct action by nephrotropic poisons on the renal tissue. Mainly affected are the proximal portions of the nephron, where the reabsorption of toxic substances filtered through the glomerules mainly takes place. Dystrophic-degenerative changes of the tubular epithelium develop even to the stage of necrosis (excretive necronephrosis). The second one relates to disorders of renal hemodynamics following the disturbance of systemic circulation in response to chemical trauma. Disturbance of renal circulation leads to kidney ischemia which results in damage to the tubular apparantus. In chronic poisoning with nephrotropic poisons transient proteinuria, cylindruria and microhematuria are observed. As a rule, the excretory and concentrating functions of the kidneys do not suffer, or change insignificantly.

Belonging to the second group are mainly binuclear aromatic amino compounds (benzidine, dianisidine, alpha and beta-naphtylamine), used in the production of organic dyes. The entry of these compounds into the organism over a long time may cause diseases of the urinary tracts. These disorders can be manifested in the form of chronic irritation of the mucosa of the urinary bladder, hemorrhagic cystitis, benign (papilloma) and malignant (cancer) tumours of the bladder.

The poisons predominantly affecting the nervous system are metallic mercury, manganese, arsenic compounds, carbon disulfide, tetraethyl lead, many narcotic substances.

Under exposure to low concentrations of chemicals the formation of the pathologic process is associate with the development of compensatory-adaptive reactions of the organism. This process is formed gradually against the background of the exhausting adaptation mechanisms. Clinical symptoms of the process are few, the process takes a torpid course and shows poor reversibility even many years after discontinuation of the contact with toxic substances.

The clinical picture and the degree of intoxications depend on the toxicological properties and concentrations of the substances, their tropism to certain structures of the central and peripheral nervous systems. The severest poisonings are caused by the substances easily permeating through the blood-brain barrier by blocking the enzymatic processes so essential in the regulation of homeostatic functions.

In chronic intoxications the main clinical syndromes indicating the involvement of the nervous system are the syndrome of vegetovascular dysfunction, the asthenovegetative or asthenoneurotic syndrome, frequently complicated by neurotic reactions.

As far as toxic encephalopathy is concerned (organic lesion of the brain), it occurs at present predominantly in blurred forms described as the asthenoorganic syndrome, when against the background of toxic asthenia neurological microorganic symptoms are revealed. Mostly affected in encephalopathy are the stem portions of the brain: stem-vestibular, cerebellovestibular and hypothalamus-stem structures, extrapyramidal formations, and this is why in toxic encephalopathy a number of basic syndromes may be singled out pertaining to the predominant lesions of the nervous system or their combinations, including the cerebellovestibular, hypothalamic and extrapyramidal syndromes.

The hypothalamic syndrome occurs rather frequently in toxic affections of the nervous system. The extrapyramidal syndrome develops as a sequence of a lesion of the striopallidal system and it is first of all typical of chronic manganese intoxication.

Rather steadily observed in pronounced forms of chronic neurointoxications, against the background of the enumerated neurological syndromes, are various psychopathological disorders whose isolated development, however, in most known neurointoxications is hardly probable.

Isolated disorders of the peripheral nervous system in the form of polyneuropathies in chronic intoxications occur rarely.

Many current forms of chronic neurointoxications are characterized by a vegetosensitive form of polyneuritis (vegetative and vegetosensitive polyneuritis) with the clinical picture dominated by vegetotrophic disorders, with a diffuse decrease of pain sensitivity, frequently following the polyneuritic type.

At exposure to low concentrations of toxic substances the clinical symptoms of intoxications are known to lose their relative specificity, macrosymptoms disappear, atypical forms are often observed, thus making timely detection of chronic intoxications very difficult. In this connection a study of contemporary forms of intoxications, their clinical features, pathogenesis, early diagnosis is an urgent task of occupational pathology. Various tests have been proposed in recent years aimed at early detection of occupational intoxications. Great importance here is attached to certain changes in the activity of various enzymes, changes in the concentration of serum proteins and their composition, to chromosomal aberrations, morphological and physico-chemical changes of blood cells and neurophysiological shifts in the activities of the central nervous system and various analyzers. Great attention is given to psychophysiological investigations. The proposed indices and tests are however often non-specific with regard to the intoxications concerned. At the same time the quantitative characteristics of the established changes may be relatively specific provided the values of these or other indices were established before exposure to the toxic substance. The diagnostic value of these or other deviations may be significant only on the condition that the data obtained are compared with the results of examining adequate control groups and with regard to the entire range of inf ences in the development of these deviations.

An increasing rate of the development of chemical industry, a continuous rise of production, the use and synthesis of new chemical substances and also the development microbiological industry accompanied by an increase of incidence of allergic diseases determine an urgent character of studying occupational allergoses including bronchial asthma.

At present as a result of the studies using up-to-date immunological and allergological methods, valuable data were obtained on etiology, pathogenesis, clinical features, diagnosis and prevention of occupational allergoses (skin diseases, allergoses of the upper respiratory tracts and bronchial asthma). However the task of finding specific diagnostic tests in this problem requires improvement of methods of allergological diagnosis, a search for the most safe and informative diagnostic techniques with the introduction of new immunological and biochemical methods and an increase of the number of chemical allergens used for diagnosis.

One of the important tasks is to elucidate the role of industrial chemical substances in the development of the most common diseases. This concerns first of all functional disturbances of the nervous system, arterial hypertension, ischemic heart disease, etc. observed under a long exposure to the action of chemicals.

Only long-term prospective epidemiological examinations of the organized population by using standard methods of investigation and unified criteria of their evaluation make it possible to determine the role and involvement of this or that effect in the development of these diseases and to reveal peculiar features of their course.

Of great importance is the problem of occurrence of tumours following exposure to toxic substances and their prevention.

The study of remote effects of toxic action is a promising trend. These studies will make it possible to reveal certain regularities in the course of occupational diseases, to evaluate whether therapeutic tactics at different stages of the disease is right, to improve disability examination and social-occupational rehabilitation.

Prevalence at present of the so-called "minor" forms of occupational intoxications determines urgency and need for elaboration of new methodological approaches during examination of the working capacity of patients with occupational diseases and solving the problems of medical and occupational rehabilitation.

At the present stage the problems of increasing the quality and optimization of medical examinations as well as the problems of scientific substantiation of the system for organizing dispensary screening of industrial workers and patients with occupational diseases acquire great importance. The main goal of this trend is to create a scientifically based system of occupational selection for work in certain professions, with regard to diverse factors of production conditions and individual peculiarities of the organism. The search for more economical and efficient methods of periodical examinations is necessary.

The studies of recent years showed expediency of stepwise organization of examinations that permits one to simplify and make initial stages of examination cheaper and owing to this to extend the methodical complex of examining persons suspected of having occupational diseases.

Solving the above-mentioned tasks will undoubtedly contribute to a further decrease in the incidence of occupational and other common diseases, more active social and occupational rehabilitation and improvement of health of industrial workers.

THE PROBLEM OF ACUTE POISONING IN CLINICAL TOXICOLOGY

E. A. Luzhnikov

In the modern world acute poisoning accounts for at least 10 per cent of all emergency cases admitted to hospital, and for some 25 per cent of the very high accidents rate whose total number of victims comes third after cardiovascular and oncological diseases (J.F. Winchester et al., 1978). In the 1970s the number of patients admitted to hospital for acute poisoning in Western Europe came to about 2 per 1000 of the population a year, as compared to 1 per 1000 in the 1960s (WHO Chronicle, 1966; S. Moeschlin, 1979). Thus, for the number of hospitalized patients acute poisoning is on a par with such a widespread affliction as myocardial infarction, and the number of its victims is greater than the number of those killed in road traffic accidents.

The incidence of acute poisoning is growing in all countries exceptionally due to domestic poisoning, which accounts for more than 95 per cent of cases, and this makes it necessary to study the causes of the prevailing "toxic situation", which we subdivide into two basic categories: "objective" ones, not depending on the victim's actions, and "subjective", directly dependent on them. An important place among the former is steady growth of the total amount of chemicals used in production and in the home which at present exceed 6 million designations. Among them are numerous medicinal preparations and cosmetic substances, household chemicals, insecticides, industrial, vegetable and animal poisons. The "subjective" causes are connected with the intensive rhythm of contemporary life which compels many people to constantly use soporifics and sedatives, which present a "factor of risk" of possible intoxication. Also included are such factors as widespread chronic diseases, such as alcoholism and drug addiction, which have long become a veritable scourge among the youth in capitalist countries.

In the Soviet Union in recent years the population has summoned emergency aid because of acute poisonings at the rate of 1.0-2.8 per 1000 people (an average of 2.0 per 1000). It has been established that from 44 to 60 per cent of these patients are hospitalized, while the number of hospital admissions varies from 0.5 to 1.6 per 1000 population (an average of 1.1) (M.A. Rogovoi et al., 1982).

The difference in the two cited indices shows that the incidence of acute poisoning depends to a certain degree on local conditions - the extent to which chemicals are used for domestic needs, the availability of medicinal preparations, the prevalence of harmful habits, etc. Such conditions usually prevail in large cities with populations in excess of half a million, where the number of calls for medical aid and of hospital admissions because of poisoning is always higher than the average.

The mean lethality rate in acute poisoning is 8 per cent, but it varies considerably in different towns and hospitals depending on the prevailing type and severity of poisoning, the age composition of the victims. In specialized centers and resuscitation wards, where the concentration of patients with severe poisoning is much higher, the fatality rate reaches 10-15 per cent.

The most widespread type of acute poisoning in this country is poisoning with medicinal drugs (mainly psychotropic), burning fluids (acids and alkalis), organophosphorous insecticides (Dipterex, Malathion), alcohol and its substitutes. These kinds of poisoning account for more than 75 per cent of this affliction.

The number of hospital beds required for treating patients with acute poisoning is 2.5 per 100,000 population. Thus, a city with a million population should have a specialized ward with 25-30 beds (8-10 for resuscitation and intensive therapy and the rest for rehabilitation) (M.A. Rogovoi et al., 1982).

The many-year experience of specialized departments (poison control centers) that were organized in many countries of Europe and America in the 1960s demonstrated their unquestionable advantages in providing high-quality aid to victims (E.I. Chazov, 1982; M.S. McIntire, 1983).

The further development in this country of a system of specialized medical aid for acute poisoning (authorized by the appropriate regulations of the Ministries of Health of the USSR and the Russian Federation) envisages the following measures:

- the establishment in all cities with a population over 500,000 of specialized departments (centers) for the treatment of poisoning in the city concerned and for carrying out preventive measures, and also consultative, organizational and methodological work in their respective area (region or territory);
- in towns and cities with a smaller population and in the countryside patients with poisoning should be hospitalized,

depending on the severity of their condition, into resuscitation and intensive care wards manned by personnel purposely trained in clinical toxicology, or to somatic (pediatric) wards maintaining permanent contacts with the regional center.

The specialized poison control department (center) incorporates resuscitation and intensive care wards, an operating theatre for carrying out artificial detoxification (dialysis, sorption), general rehabilitation wards and a laboratory.

A specific feature in the diagnosis of acute poisoning is the need for urgent detection of toxic substances in the bio-environments of the organism for which special laboratory examinations are undertaken with the aid of rapid instrumental methods (gas-liguid chromatography, spectrophotometry, etc.). This allows to determine, firstly, the kind of toxic agent present and its concentration in the blood, which directly correlates with the symptoms and the prognosis of the poisoning; secondly, the stage of the poisoning, largely determining the scope and kind of treatment given the patient.

Our studies of recent years, based on clinical and laboratory observations of more than 1,000 patients with various kinds of poisoning have made it possible, with the aid of computers and systemsanalysis, to determine the threshold, critical and irreversible blood content levels for many toxic substances that were identified on the patients' admission to hospital 2-3 hours after poisoning had taken place (see Table 1). At the threshold level a variety of clinical symptoms is observed, but their outcome is usually favorable, since the intensity of the "chemical damage" does not exceed the organism's compensatory potentials. At the critical level the prognosis is uncertain, since it largely depends on other factors, above all, on the time and scope of medical aid, the patient's age, etc. At the irreversible level of poison concentration in the blood the poisoning usually has a fatal outcome due to the intensity of the "chemical damage" being incompatible with life. The clinical picture of poisoning and quantitative indices of homeostatic disorders changed in accordance with these levels.

Table 2 presents the correlation between the content of Malathion in the blood and the main quantitative indices of the body's response.

At a "threshold level of acute poisoning" changes occur in the indices reflecting the selective toxicity of the poison (diminished activity of blood cholinesterase). No substantial changes are observed in systemic hemodynamics and the acid-base equilibrium in this group of patients.

When the blood poison content reaches a critical level the outcome of the poisoning becomes uncertain, while the indices of the organism's overall response already differ considerably from the norm. The most pronounced disorders of homeostasis took place at the irreversible level of Malathion concentration in the blood. This transition from the primary toxic effect to irreversibility should be regarded as a number of successive stages in the disruption of the adaptation process, one of whose stages is the failure of the adaptive mechanism and development of a "critical state".

Therefore, an analysis of the "poison concentration -- toxic effect" correlation allows to objectively assess the quantitative aspect of the relationships between the poison and the organism, which is of tremendous practical importance for timely diagnosing "critical" states and selecting adequate treatment.

There are certain specific features in the nature of the critical states in different kinds of acute poisoning, reflecting the agent's selective toxicity. For example, in OPI poisoning the fatal outcome is related to manifestations of its muscarine-like effect (bronchorrhea, bradycardia), nicotinic effect (hypertension and respiratory paralysis), the poison's central action (coma, respiratory paralysis, convulsions). Aggravating the unfavourable outcome in acetic acid poisoning are symptoms reflecting the poison's destructive action (chemical corrosion of the stomach, intestine, upper respiratory ways), the resorptive action of the poison (intravascular hemolysis) and the neural-pain factor (exotoxic shock).

In barbiturates poisoning the onset of death is related mostly to the narcotic effect on the central nervous system (comatose condition) and its vital centers (respiratory paralysis).

In addition to the aforementioned symptoms of poisoning, reflecting the selectiveness in the toxic action of the poisons, a critical state may arise also due to the development of various nonspecific complications (e.g. tracheobronchitis, atelectases, pneumonias, etc).

One should note that the significance of all this variety of clinical manifestations of intoxications for an unfavorable outcome is not the same. A comparison of correlation coefficients indicated that a decisive element in the onset of irreversibility in dichloroethane poisoning is exotoxic shock, in

OPI poisoning -- respiratory disorders (in the form of respiratory paralysis and bronchorrhea), in barbiturate poisoning -- narcotic coma, and in acetic acid poisoning -- chemical corrosion of the stomach followed by the development of shock, gastroesophageal hemorrhages and intravascular hemolysis.

There exists, therefore, the kind of critical state specific to each type of toxic substances which is of certain importance for the practical activities of physicians, since it allows to concentrate attention on the priority detection and therapy of these, most dangerous manifestations of the intoxication.

If the specific clinical features of poisoning are studied in relationship to the kinetics of the poisons concerned, one may note that certain periods of poisoning substantially differ in the nature and combination of symptoms contributing to the formation of an unfavourable outcome. These differences are quite clearly observed when comparing the first and fourth days of the disease. For example, in dichloroethane poisoning the symptoms which determine the development of the death process during the first 6 hours of intoxication (narcotic coma, respiratory disorders, exotoxic shock) are no longer involved in the thanatogenesis on the fourth day and, on the contrary, the symptoms which by this time revealed a connection with the development of an unfavourable outcome (toxic nephropathy, pneumonia, toxic psychosis) have not yet taken shape in the early period of intoxication.

The data obtained made it possible to single out two basic stages (phases) in the course of the toxic process: the toxicogenic and somatogenic ones.

The toxicogenic stage corresponds in time to the period when the poison is present in the organism; it is characterized by the appearance of those symptoms of intoxication which reflect the "selective toxicity" in the poisons' effect on certain organs or systems.

During the toxicogenic stage of acute poisoning methods of "early" diagnosis, which are of the nature of an etiological influence, are of the greatest importance. This influence is most effective when the poison's toxicokinetic features are taken into account. Its success often depends on vigorous therapy of exotoxic shock.

The somatogenic stage sets in when the poison has been actually completely eliminated. In this period the severity of the patients' condition is due to the consequences of the chemical injury sustained, which most frequently include pneumonias, toxic hepatopathies and nephropathies, trophic disorders, toxic psychoses, somatogenic collapse, etc.

During the somatogenic stage non-specific therapy assumes pre-eminent importance. Aimed at coping with developed homeostatic disorders, it proves more effective when the poison's toxicodynamic features are taken into account. Often quite essential in the complex of therapeutic measures are methods of late detoxification for controlling endogenous toxicosis, developed because of functional insufficiency of the liver and kidneys, burns, severe hypoxia and infectious complications (pneumonia, sepsis).

When treating exotoxic shock it is important to bear in mind its pronounced oligemic character, and also the possible development of a hyperdynamic or hypodynamic state of the circulation which may alternate in one and the same patient (for example, in heavy soporific or OPI poisoning). The correction of steep drops in peripheral vascular resistance observed during this kind of poisoning requires, after restoring the lost plasma, lasting administration (for 10-12 h) of pressor amines -- norepinephrine and dopamine.

Among detoxification methods indicated in the toxicogenic phase only, mainly used at the threshold level of intoxication, is forced diuresis, and at the critical level - hemosorption conducted in intermittent sessions of 25-30 min until the concentration drops below the critical, and also hemodialysis. Our experience in the clinical application of hemosorption for the treatment of acute intoxications is represented in Table 4. At irreversible levels of poisoning when symptoms of decompensated shock developed, one may use peritoneal dialysis since hemosorption and hemodialysis are contraindicated at low arterial pressures.

Pharmacological detoxification methods include the administration of antidotes which help to protect vital systems of the body for the time necessary for the removal of the poisons by methods of artificial detoxification. Unfortunately, there are very few effective specific medicinal agents, while their administration is limited to the toxicogenic phase of intoxication. Most frequently used as antidotes are cholinolytics (atropine) and cholinesterase reactivators (dipyroxime) in cases of OPI poisoning.

In the last 5 to 10 years clinical practice has encountered new types of acute poisoning whose clinical aspects and methods of treatment are still very little known to the practicing physician. Concerning medicinal agents there has been an increase of poisoning with amitryptyline, which possesses a pronounced cardiotoxic action manifested in disorders of rhythm and heart conductivity of the type of intraventricular block and fibrillation. Also on the increase in the number of intoxications with a mixture of various drugs, particularly psychotropic, potentiating each other's toxic effects. Numerous cases of grave toxic nephropathy have been caused by incorrect administration of blue (diluted mercurial) ointment.

In the group of organophosphorous insecticides (OPI) Malathion came to occupy the first place; oral poisoning with it proceeds rather severely with early development of exotoxic shock.

Also on the increase has been the number of poisonings with automobile exhaust fumes causing the development of toxic encephalopathy and the myorenal syndrome. In the group of alcohol substitutes there is an increase in poisoning with acetone and higher alcohols causing severe metabolic acidosis. Besides, with the elaboration and introduction into clinical practice of new diagnostic and therapeutic techniques, the ordinary clinical course of acute intoxications and the nature of their complications have notably changed; this may be designated by the term "clinical pathomorphosis", which reflects "morphological pathomorphosis", noted by the pathoanatomists (N.K. Permyakov, 1979).

6300 8

The overall pathogenetic cause of "clinical pathomorphosis" of chemical diseases is the definite shortening (1.5-2 times) of the toxicogenic period of intoxications owing to the broad application of such artificial detoxification methods as hemodialysis and hemosorption.

Table 1. Blood Poison Content as Criterion of Severity of Poisoning

Toxicant	Threshold level, µg/ml	Critical level, µg/ml	Irreversible level, µg/ml
Malathion	0.01-0.17	0.2-1.5	over 1.55
Dipterex	0.02-0.8	0.9-9.0	over 12.0
Methyl parathion	0.05-0.29	0.33-1.1	over 1.2
Phenobarbital	21.0-49.0	50.0-102.0	over 102.0
Dichloroethane	traces	0.14-0.86	over 1.0
Acetic acid (free hemoglobin concentration in plasma)	5.0-5.6	5.8-20.6	over 21.00
Patients	surviving	outcome uncertain	fatal outcome

Table 2. Correlation between Blood Poison Content and Body Response Values in Malathion Poisoning

Physiological indices (units)	Threshold level	Critical level	Irreversible level
Blood poison content (µg/ml)	0.01-0.17	0.2-1.5	1.55-1.9
Cholinesterase activity in whole blood (% to norm)	57.08±3.8	31.48±1.55	3.89±1.3
Increase of ECG systolic index (%)	4.26±0.95	10.0±2.4	16.6±1.9
Mean arterial pressure (mm Hg)	normal	68.45±4.12	47.56±12.62
Stroke volume of blood (ml)	normal	51.18±3.41	31.0±4.75

Table 3. The Use of Hemosorption in Exogenic Poisoning (N.V. Sklifosovsky Scientific-Research Institute of Emergency Care)

Procedure	Poisoning agent	Clinical effect +++ - intense ++ - moderate + - mild	Clearance, ml/min
1. Hemosorption (Sorbents SKT-6a, SKN, BAU)	1. Psychotropic drugs	+++	(48-283.5) 3±8
	2. OPI	+++	(35-116.2) 42.4±12)
	3. Alkaloids	+++	(44±7) 66±2
	4. Salicylates	+++	66±2
	5. Dichloroethane	++	(78-121.6) 38±12
	6. Heavy metals	+	-
	7. Amitrytyline	++	49±3
	8. Ethylene glycol		
2. Plasmosorption (Sorbents SKT-6a)	1. Medicinal agents	+++	(66-83) 78±5
	2. OPI	+++	(35-54) 44.5±4
	3. Dichloroethane	++	-
3. Hemosorption at prehospital stage (Sorbents SKT-6a, SKN)	1. Soporifics	+++	-
	2. OPI	+++	-
	3. Dichloroethane	++	-
	4. Amitrytyline	+++	-

REFERENCES

1. Luzhnikov E.A. et al. Osnovy reanimatologii pri ostrykh otravleniyakh (Principles of Resuscitology in Acute Poisoning). Moscow, Meditsina Publishers, 1977, 360 pp. (in Russian).
2. Luzhnikov E.A. et al. Anesteziologiya i reanimatologiya (Anaesthesiology and Resuscitation). 1980, 6, 57-62 (in Russian).
3. Permyakov N.K. Osnovy reanimatsionnoi patologii (Principles of Resuscitation Pathology). Moscow, Meditsina Publishers, 1979, 279 pp. (in Russian).
4. Rogovoi M.A. et al. Sovetskoye zdravookhraneniye (Soviet Public Health), 1982, 1, 16-20 (in Russian).
5. WHO Chronicle, 1966, 20, 1, 3-13
6. Chazov E.A. "Terapevticheskii arkhiv" ("Therapeutic Archives"), 1980, No. 10, 3-6 (in Russian)
7. McIntire M.S. N. England J. Med." 1983, 308, No. 4, 219-22
8. Moeschlin S. Klinik und Therapie der Vergiftungen. Stuttgart, 1972
9. Winchester J.F., Gelfand M.C. and Tilstone W.J. "Drug Met. Rev." 1978, 8, 1, 69-104.

Chapter XIII

INFORMATION SYSTEMS ON CHEMICALS; HAZARDS AND RISK ASSESSMENT

Edited by A.V.Butrimenko,
Doctor of Sci.

THE USE OF COMPUTERS IN COLLECTING AND PROCESSING INFORMATION ON TOXICITY AND HAZARDS POSED BY CHEMICALS

A. V. Butrimenko

Computerised information processing based on present-day hardware, software and information switching facilities has found wide use in the past few years. Specifically, the latest developments in the field include the use of on-line computer systems and computer networks providing access of many users to each system and of each user to many systems. Information processing is usually divided into two types: computations, including calculation of various scenarios using simulation models, and information searching in data banks. The computer network structure covering both computer-based services and the corresponding communication network is schematically shown in Fig. 1.

Let us consider two types of resources: the resources united by the network, and the basic and secondary resources which are of the principal interest for users. The secondary resources are necessary for the integration of the basic resources represented by the data communication network.

The resources of the first type (primary resources) include:

(1) computer resources - processors and working memory;
(2) mass memory - disks and tapes;
(3) input-output devices - printers, displays, plotters, etc.;
(4) data packages;
(5) applied software;
(6) computer personnel.

Secondary resources providing access to secondary resources embrace:

(1) communication lines and modems;
(2) switching nodes and concentrators;
(3) network software or the network operational system; and
(4) the network managerial personnel.

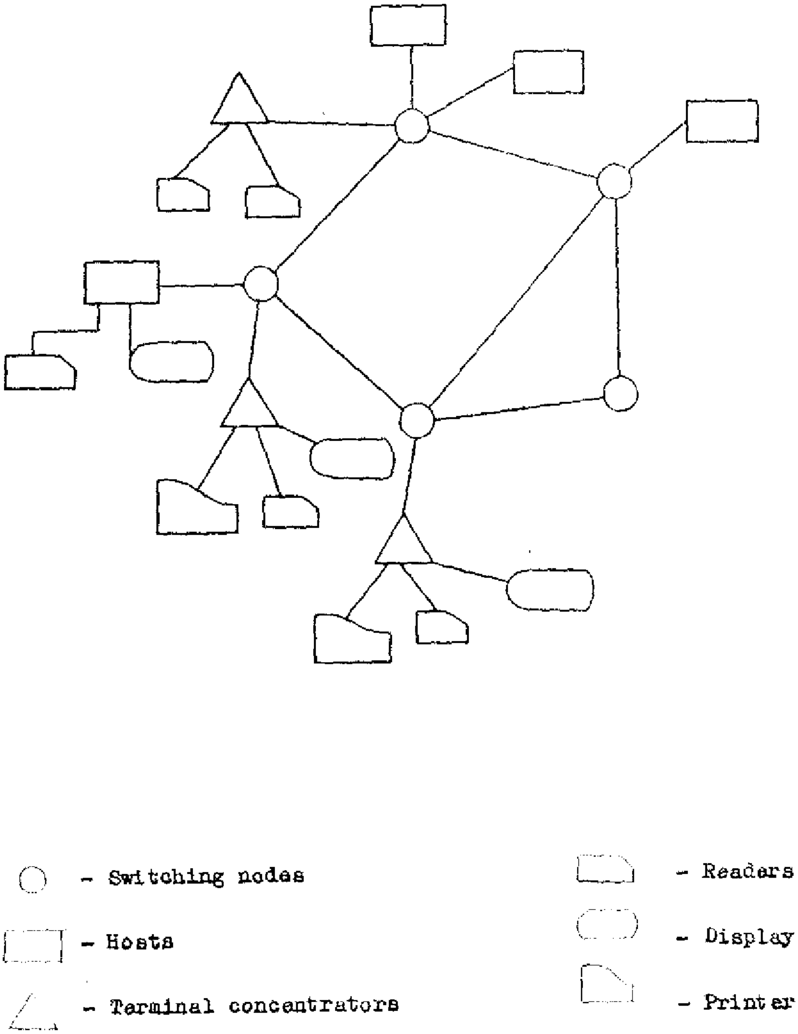


Fig. 1. A diagram of the computer network structure

Tendencies in developing these two types of resources are considered starting with the network resources.

Integration and sharing of resources, including communication computer resources, and skilled personnel is the main factor common for all computer networks.

Integration and sharing of resources is not a new phenomenon neither for communication where time and frequency compression, group formation, enlargement of bunches, etc. are a common practice, nor for computer technology where the more effective use of computer resources by their shared use in the multiprogram and time-sharing mode.

The initial advances in expanding computer networks were based on the integration within one system or computer network two principles of resource sharing; packet switching, and time-sharing. Packet switching improves considerably the communication recources efficiency due to the use of fast communication channels (as compared with the division of a wide band into several low-grade telephone channels) and also due to queueing information packets. Queueing, in principle, delays information delivery which occasionally may reduce the system efficiency, especially when long messages are to be transmitted. At the same time, the time-sharing mode whose part in the total amount of data processing is growing steadily, leads, however, to exchange of relatively short messages requiring the same delay time for all messages.

Computers are usually divided by their cost into three classes; small, medium, and large.

Two facts - retention of the share of large computers at a 5% level and a drastic increase in the share of minicomputers - are of special interest here. Statistical data show that in 1978 minicomputers amount to 60% of all computers. It is quite possible that their share would increase up to 80%.

The unchanged share of large computers may be explained by a considerable and constantly growing number of problems requiring for their solution large, often extreme, computer capabilities. The fact that minicomputers became cheaper and much more effective, and especially the advent of operational systems where minicomputers can be used in the time-sharing mode, have contributed to the dramatic increase of their share in the total number of computers. A relatively low cost of minicomputer service explains to a large extent their success on the market.

Minicomputers are widely used also because they can perform new operations, especially those connected with handling observation results and setting up small-scale information systems. Thus, the changed share of computers on the market is not only indicative of new capabilities of computers themselves, but also a consequence of the changed functions performed by computers.

Availability of commercial minicomputers increased the number of users having direct access to computers. At first sight the tendency appears to be opposite to the development of computer networks. Actually, however, expansion of computer networks and the wide use of minicomputers are "two sides of the same medal".

Computer facilities are developing towards ensuring the more effective "man-machine" interaction and the direct data input into computer. In this development trend the contribution of host computers to overall information handling effort is declining. Thus, in the mid-1970's the share of expenditures on host computers amounted to 30% whereas for the past decade it has dropped to 23% mainly due to wider use of communication equipment.

Let us consider development trends for individual components of the hardware and its cost. The amount of direct data input from display keyboards has increased markedly.

Already now many computer centres have no punch tape and punch card readers. In this context it is worth noting that amount of input data from sources and outside computers has increased considerably.

The role of both software and hardware in computer operation has changed radically. Nowadays cost of software for users more often than not exceeds cost of hardware. Thus, for example, expenditures for the software meant for manned flights within the framework of the NASA programme amounted to one billion dollars in the period from 1960 to 1970.

Examples are found in the changed share of hardware cost in the overall computer expenditures of the US Defence Department, where they dropped from 50% in 1968 to 20% in 1974.

Great sums of money are alotted for devising operational systems and applied software. For example, the operational system for IBM-360 computer cost 200,000,000 dollars of which half was spent on debarging and test, R&D cost proper was 33% and programming cost - 17%.

Development cost of the operational system for the computer network itself, as far as the ARPA system is concerned, exceeded 20 million dollars.

Despite the growing expenditures on commercially available software a greater share of it, especially applied software, continues to be devised at computer centres to meet their own needs.

Analysis of programming policies pursued by state organisations in the United States showed that 65% of all programs had been prepared by the centres themselves, 9% - received from computer manufacturers, 11% - from independent software generators, 11% - from the system suppliers, and 4% - from other sources.

Despite the constant growth of software cost, its increase is uneven for computers of different classes.

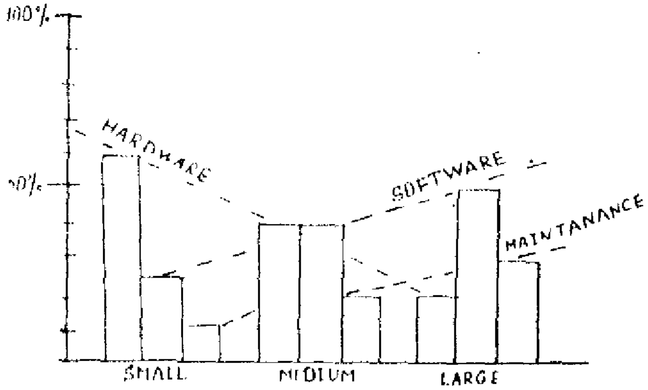


Fig. 2. Cost of hardware, software and services for the three types of computers

Fig. 2 shows expenditures on hardware, software and service of computers of three classes. Shortage of skilled manpower, the size of which is itself a rather impressive resource, is one of the crucial factors holding back the use of computer technology. Table 1 shows number of system programmers and installed computers in the United States. The data show that in spite of the sharp decrease in the share of system programmers as compared to number of installed computers, the numerical strength of system programmers continue to increase because the rate of computer growth exceeds the pace of "rationalisation" of system programmers efficiency. Moreover, the marked decline in the number of system programmers for one computer, which took place during 1970-1975, was followed by the same rate of decrease this is almost two-fold for 1975-1980. During the next five-year period this rate of decrease is expected to low down considerably, the programmer/computer ratio will change only slightly while the number of computer will continue to grow at the same pace.

Some 400 men of service personnel were employed in the FRG computer centres in 1978.

Table 1. Number of programmers in the USA

	Computer	Programmers	Prog. per computer
1955	1,000(?)	10,000(?)	10(?)
1960	5,500	30,000	5.5
1965	22,500	80,000	3.6
1970	70,000	165,000	2.4
1975	225,000	220,000	0.98
1980	700,000	275,000	0.39
1985	1,1000,000	330,000	0.30

Special attention should be drawn to cost of workforce since the optimal use of skilled personnel is particularly important and not only because this resource is costly but also because it is depletable. Thus, about 1.5 million men are currently employed in computer manufacturing and servicing companies in the USA.

According to M. Rakovsky estimates (I) the figure for the USSR is 600,000 of which almost half is working in computer centres and another half - in the computer manufacturing industry.

It is important here to keep in mind that a relationship between the number of computer personnel and the number of computers in operation is determined by the intensive use of computers in the national economy. The need to employ such a big resource as computer service personnel is one of the factors which limits the wide use of computers and determines to a great extent their use efficiency.

The share of payroll cost already now has reached 46% and will continue to grow to exceed before long 50% of the total expenditures of computer centre maintenance.

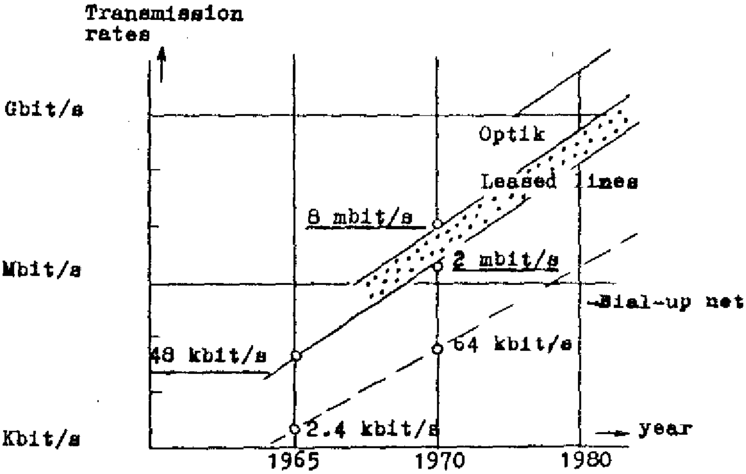
It is possible to ascert, therefore, that the present-day computer centre is a complex and rapidly expanding resource in which manpower is most costly, then comes software and then hardware. In the hardware itself the role of host computers is decreasing and the role of input-output devices - increasing.

Let us now discuss in brief some of the specific features in the development of secondary resources directly involved in the use of basic or primary resources.

To show their development rate and importance it is sufficient to say that in 1978 user expenditures on data transmission exceeded in the USA expenditures on data processing and in 1980 income received by the American Telephone and Telegraph Company (TTC) from data transmission overcame income from conventional telephone services. The existing 5.5 billion dollar market will grow up to 12 billion dollars in 1985. The market is represented by three sectors: transmission of digital information proper through communication channels; processing of information prior to its transfer, this is data transmission and storage in communication nodes; and conversion of message transfer speed, conversion of information formats, conversion of data transfer means, conversion of discrete signal flow into a form convenient for reading and, vice versa, conversion of texts into a flow of signals.

The rapid expansion of the data transmission market is accompanied by even swifter growth of expenditures on conversion of formats, transfer speed, etc. This is especially true of conversion of primary information into a form suitable for data transmission through communication channels and, vice versa, into a form convenient for users. It is expected that in 1985 conversion costs will be equal to costs of information transmission and information processing taken together.

, Fig. 3 shows engineering possibilities of attaining various speeds of data transmission depending on types of communication channels, as well as message speed-quality relationship.



ıion

Fig. 3. Technical capabilities of increasing data transmission speeds.

Nowadays data are usually transfered through cables, though significant progress has been made in the use of radio-channels provided by satellites. In the next few years radio communication channels for packet information switching will, apparently, be used on a wider scale. However, hardware alone cannot ensure the adequate standard of user service.

As we already mentioned above, the use of so-called packet switching, which helped to reduce both cost and time of information delivery, has opened up new vista for computer networks.

Information transmission cost in message switching networks is determined by two factors: the communication channels used and packet switching with the help of minicomputers. Effect of these two factors on information delivery cost has been studied in detail with special reference to the ARPA network. The analysis showed that processing of 10 information packets cost 0.168 dollar in 1970 as compared with 0.22 dollar spent for transmission of the same amount of information. In 1974 transmission cost reduced to 0.12 dollar whereas processing cost decreased to 0.026 dollar. The comparison shows that greater efficacy of computers in information switching networks was the main factor of lowering information transmission costs.

The rapid expansion of computer networks both at national and international levels has moved to foreground differences between the existing legislation and practical experience in using new data processing and information switching facilities.

The development and operation of computer networks have made it necessary to devise a new organisational and technical structure of management, including:

(1) technical standardisation to ensure compatibility between the computer and information switching capabilities, coordination of "protocols", compatibility of terminals used, etc.;

(2) financial control, including pricing of different services and drafting tariffs for data switching operations;

(3) legistative regulation of information collection, use and transmission on both national and international scales.

Since first computer networks were pilot type, technological progress in the field has by far overtaken the establishment of the adequate economic and legislative machinery. At the same time, discussion and adoption of technical standards regulating data transmission have revealed wide disagreements between two groups of companies - manufacturers of communication equipment and manufacturers of computer facilities. Communication departments were also active in drafting and adopting standards. In 1976 standard X.25, which is in fact a set of standards, was adopted. It proved to be more advantageous for communication departments since the computer facilities in users' hands and the data transmission networks under the communication departments' jurisdiction have been divided so that most functions are supposed to be fulfilled by the network whereas the users have relatively limited rights. As a result greater part of computer network equipment is referred to as communication facilities.

Several big companies, including IBM, had been tried for a long time to ignore effort to adopt standard in the communication field. Nevertheless, by the early 1977 most manufacturers of computer facilities and communication equipment had awared the need and usefulness of adopting such standards, IBM also declared that it had adopted international standard X.25.

In contrast to the introduction of technical regulation that required a relatively short period of time for its realisation, the economic and legislative control is still far from its practical implementation. Here we observe a dramatic tangle of interests of the national security, and national concerns in development and protection of national industry.

The US laws regulating the use of data transmission and computer networks differ greatly from respective laws in West European countries. The United States policy in the field has been expounded at four crucial meetings of the Federal Communications Commission. In the First Computer Inquiry (1966--1971) government-controlled telecommunication services were separated from "uncontrolled" data processing services. In compliance with this division "message switching" became a responsibility of public networks because their basic function was information transfer. Consequently, information processing companies were not supposed to offer message communication services. This requirement caused great concern among several companies. As a remedy the decision on "public service" adopted in 1969 and amended in 1971 permitted companies specialising in information processing to provide communication services in competition with "traditional" public networks, such as American Telephone and Telegraph Company (AT?) and Western Union.

In this decision "public networks" have been expanded to include such systems as TYMENET and TELETEN which have no primary network of their own. The decision on "reselling and task-sharing" adopted by the US Federal Communications Commission introduced a new division between the information processing services operating a data transmission system as their integral part, and communication services engaged in reselling basic communication services represented by the companies which buy basic communication resources from owners of primary public networks and then resell their services. Besides the decision has specified the services which should be provided by major public networks of the ATT type for the primary communication network.

The networks of the new type became known as "value added networks", unlike the usual services offered by traditional communication networks, value added networks, such as TELENET, provide for the adaptive multiplexing of channels, searching, and establishing connections with computer services or information transmission through the optimum channels, error detection and correction, conversion of message transmission speeds and codes, joining different computers and terminal to the network.

The Federal Communications Commission explained also that "communications companies" were taken to mean the companies operating primary communication networks and companies reselling communication services. However, no satisfactory definition of the term "data processing" has been suggested. "The Second Computer Inquiry", which appeared in 1976, contained a wider definition of the term "information processing" embracing also information transmission at which:

(a) information content or input information meaning has been somehow modified, or

(b) output information is an answer to input information obtained with the help of a program.

In Western Europe the laws regulating the use of computer networks and data transmission networks differ from respective laws in the United States mainly by the fact that in most West European countries the networks belong to the state and are controlled by communication departments which directly receive income from information transmission services provided. Two typical responses of such communication departments can be noted here. Firstly, the introduction of additional control over the international computer-assisted information flow. Thus, French, British, Austrian and West German post offices require that access to US-owned TELENET and TYMNET should be provided only if the communications department equipment is used for which a high tax needs to be paid generally proportionally to the amount of information to be transfered. Secondly, most countries have special regulations forbidding a terminal-to-terminal information transmission, and this may stimulate competition for the telecommunication which is also under authority of the communication departments.

National communication departments played an important role in setting up high tariffs for all types of international services, including direct communication channels. This is particularly evident when we compare cost of leased lines in the USA with leased lines between Europe and the United States.

Thus, for example, the direct leased line between New York and Los Angeles costs 1090 dollars per month as compared with the New York - London line which costs 8683 dollars.

Whereas the lease and use of communication facilities is controlled by historically established barriers and mechanisms protecting national interests with varying degree of success, the legal protection of the remote and especially international use of computers has neither the historical basis nor analogy and is now at the nascent stage.

In 1976-1978 most West European countries adopted regulations or laws specifying the use of computers and message switching procedures. Despite this the legislation in the field, as the existing experience and comparison of national legislations have shown, is still far from comprehensive and adequate.

National legislations are drafted taking into account several requirements and specific conditions dictated by the following considerations:

(1) national security;

(2) economic interests;

(3) observation of personal rights and by-laws of individual organisations.

The need for new forms of national security protection can be explained by the fact that the growing computerisation has posed immense difficulties for information protection from unfair or criminal use. Information leakage is snowballing whereas counter-measures are lagging behind the computerisation drive. Great amounts of information are concentrated in a limited number of data bases. It should be kept in mind that all this information may be used for purpose different from those for which it has been legally gathered and processed.

Respective draft legislations are meant to relulate the collection and storage of data the disclosure or destruction of which may be detrimental for national security. Specifically, apart from protecting information from adverse effects, a legislative system should secure data bases from pressure of a possible economic blockade or boycott which may disrupt the smooth operation of information centres.

Several international organisations, including UNESCO and IBI, pay much attention to these problems. Moreover work is under way to assure access of all countries, especially developing ones, to world knowledge major part of which is nowadays stored in data banks and computer centres.

The expansion and the adequate protection of this sector are the matter of growing economic concern of respective countries. Since the mid-1960's, the provision of remote, including international, data processing and storage services in addition to selling and export of computers has increased drastically. West European countries have over 150 remote access systems. According to EURODATA, the amount of information transmission in Western Europe will increase 12-fold by 1985 as compared to 1977.

Nevertheless, processing, storing and remote access continue to be regulated inadequately.

The absence of national regulation in West European countries for a relatively long time became an objective stimulus for the rapid monopolisation of such services by US companies. Thus, today such US systems as TELENET, TYMNET, MARK-3 and CYBERNET specialising in selling information and computer resources have their branches in Western Europe. Profits of these companies from selling their services abroad exceeded 1.2 billion dollars.

J. Faulner, Canadian Minister of Science and Technology, said that the problem of international data flow had created a potential for growing dependence rather than interdependence which entails a danger of loosing the legal access to vital information and a danger that industrial and social development would be determined mainly by decisions and interests of groups situated in a foreign country.

He asserted also that in 1976 Canada lost 150,300 million dollars of revenue by importing computer services from the USA in addition of loss of about 30-40,000 working places in the data processing sector alone.

In this connection, it should be noted that export of information and computer services is a new trend in the international division of labour and in foreign trade since marketing of goods (information, data processing) does not result in their depletion in the country and requires practically no renewable national resources. In this area interests of West European countries, the United States and developing countries are clashing vigorously.

The differences in national interests, which manifest themselves in adopting national legislative acts against unfair use of data in a machine-readable form, can be boiled down to the following: compulsory registration of data forms, band for the collection and storage of certain type of information, protection from unauthorised access, and guarantee of access of a legal person to personal information stored in a data bank.

National data registration rules differ widely especially as regard private and public data banks. Thus, for example, in Austria it is sufficient to notify corresponding state authorities that a data bank has been set up, whereas in Norway, Spain and Sweden it is generally required (depending on a type of information) that a state license should be granted. In Austria, Belgium, France, the FRG, the Netherlands, Norway and Sweden the respective legislation requires that physical security of data should be guaranteed. In Austria, Belgium, the FRG, the Netherlands, Spain, Sweden and the USA violation of laws concerning the use and storage of data is punished as a criminal act.

Most legislative acts in force forbid any transfer, storage or processing of personal data abroad.

As we have already noted, the advent of computer networks has been predetermined mainly by appearance of so-called packet switching which paved the way for computer centre networking.

Below we shall give a brief description of packet switching and its difference from channel and message switching.

The rapid channel switching using, as a rule, a telephone line is the situation when two subscribers are connected with each other through a compound channel comprised of several transit sections assigned to the subscribers for the period of their contact. Upon completion of the contact each transit section of the compound channel begins functioning independently and can be used in forming other compound channels. A considerable disadvantage of this type of switching is that the sections assigned to a definite connection cannot be used for communication between another couple of subscribers even if the channel remains idle. This type of data switching is, apparently, especially ineffective during work in the dialogue mode which is characterised by relatively short dispatches of information with considerable intervals between two successive dispatches .

The message switching method is used in telegraphy and belongs to the class of so-called relay or store-and-forward method.

Packet and message switching methods belong to the same class. During message switching complete text reaches its destination after its successive transmissions from one node to another. With this method a message at each period of time is occupying one section of the channel connecting the source and the receiver or is stored queueing at the outgoing section of one of the nodes.

This method has the disadvantage that a message is switched as an integral whole and in stage-wise manner. Because of this reliability of received information is relatively low and no information upgrading procedure is stipulated.

During packet switching, which is also based on the relay method, a message is divided into blocks of standard length (packets) each having its own address and is treated by the network as an independent message. The standard length of each block is chosen taking into account the optimal reliability which is attained by the use of códes and repeated switching of damaged blocks.

Since a message should be transmitted from the source to the receiver without errors, additional checking is accomplished at the receiving node. Message compilation of individual blocks is called assembly and message fragmentation is termed disassembly.

The reliable information switching between two subscribers is regulated by a set of special rules or protocols.

To sum up all said above, it is necessary to point out that the use of packet switching has made it possible to build a communication system featuring a high, reliability and authenticity of switched information and this, in its turn, enabled creating an information and computer system for storing, processing and transmitting information in the form of interconnected and coordinated processes.

Work of users with data banks in the interactive (dialogue) mode is one of the basic type of computer network utilisation. It is necessary to emphasise here that the interactive mode is characterised by relatively short dispatches of information (request-answer) is very convenient for packet switching. Data banks depending on information they contain are usually divided into three types.

Bibliographic data banks contain references to a publication (article, book, report, etc.) usually complete with its abstract.

Documentary data banks contain complete documents, e.g. specifications, preprints, etc.

Factographic data banks contain information in the form of digits and often tabules.

Let us now dwell on data bank tariffs.

Customer's expenditures on the use of a data bank within the computer network consist of several components. Most expenditures are associated with data switching in the computer network. Prior to access to a computer network, this is to a telecommunication facility, the user should have a permission for access to the system in the form of a special password. One-time access to a network generally costs not more than 1.0 dollar. Payment for a communication session includes: cost of the user terminal connection to the network, and the amount of information to be transferred in terms characters (letters or digits). Tariffs differ slightly for different networks, but on the whole we may say that one minute connection to a network costs approximately 20 cents and 1000 characters transmitted through the network costs 0.6 dollar. Transmitted characters include both characters transmitted by the network user and characters received by the user from a remote computer.

Costs involving direct use of data banks include cost of time required for access to a remote computer, and cost of work with a particular data bank. This means that the existing tariffs are not generally convenient especially for unexperienced users who cannot work with the system efficiently. A number of centres today has begun using a different tariff system more responsive to the real amount of information obtained by users. To sum up we may say that one-hour access to a computer network costs from 30 to 120 dollars depending on the data banks and network used.

Many of such data banks contain direct or indirect information on toxic chemicals and their effects on both environment and human beings. One of the problems in gathering and analysing information on toxic chemicals and their environmental impacts is associated with the absence of specialised data banks for this type of information. The only exception is several national data banks containing information on household chemicals, their toxicity, and the corresponding safety measures. To glean such information it is generally necessary to scan several data banks differing one from another by query languages and thesauri.

In this connection it became necessary to set up a specialised centre with the adequate capabilities for storing information gathered from other data banks, with the necessary software facilitating query statement with subsequent query rewriting in one of the working query languages. The typical infrastructure in one of the working query languages. The typical infrastructure of such a centre may comprise a mini-computer with external memory on disks and the necessary interface for access to the network.

Such equipment will also make it possible to reduce cost due to preliminary reparation of requests and their editing.

From the engineering point of view the computer centre equipment should provide for the following:

(a) easy access to computers and data bases in the interactive and preferably packet modes, using intelligent terminals and ASCII and EBDCDIC codes;

(b) regular recording, stock-taking and reporting on all computer accesses, prevention of unathorised access to external resources (computers, computer networks, data bases, information systems) by using a system of electromechanical and programmed keys and efficient control by a monitor over the state of the software and information transmitted through any physical channel, in case of time division of communication channels (when multiplexers of a time-division channel is used) or vertual channels when packet switching is used; and

(c) establishing a local library of programs and data bases designed by users for remote computers and computer networks.

Organisationally the following administrative function performed by the centre can be singled out:

(a) providing legal and financial bases for access to external resources, including signing of contracts, agreements, commercial contracts, control over payment, writing of surveys, etc.;

(b) consulting users on how to gain access to external resources and briefing them on specific features of their effective utilisation; studying users with the aim of expanding the centre and types of services offered;

(c) executing administrative control over access and its monitoring, including organisation of operator's work with remote computers in the packet mode, recording, checking and storing of protocols (keeping the archives);

(d) setting up a local library of technical documentation, specifications and manuals on the use of external resources and operating instructions for the centre's equipment, and also expanding the library of programs and data bases designed by users;

(e) providing for the smooth operation of terminals and switching equipment (modems, multiplexers), establishment and development of the packet switching system and control over effective operation of the communication lines.

Structurally the centre can be divided into two organisationally different parts:

(a) communication part responsible for communication provision; and (b) terminal part providing easy access, user service and control over the correct use of remote resources in compliance with signed agreements and contracts.

All the above technical functions of automated access centres can be executed in two principally different versions irrespective of equipment used (Figs 4 and 5).

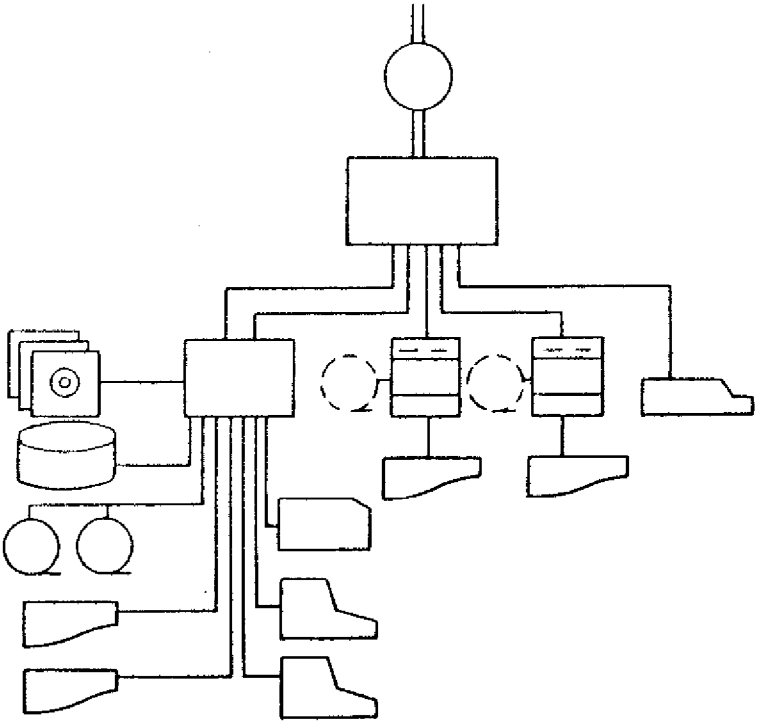


Fig. 4. Minor configuration of the computer access centre:

Expenditures on purchasing equipment according to the first configuration will make it possible to provide terminal access, communication control and the initial switching scheme which will be further expanded when the configuration shown in Fig. 5 is introduced. The configuration shown in Fig. 5 is more powerful and flexible; it can provide controlled access to foreign resources (computers, data bases, etc.) through the centre.

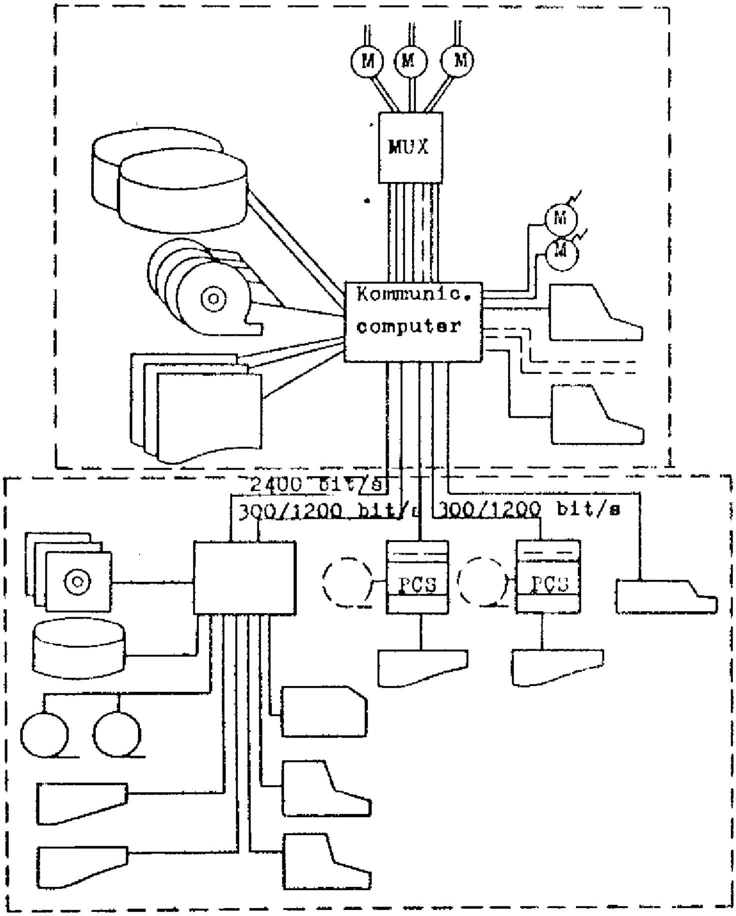


Fig. 5. Major configuration of the computer access centre:

Thus, the current analysis of the technical, legal and organisational problems of using remote access to data banks allows us to ascert that present-day communication facilities, computers and the corresponding juridical norms have made it possible to undertake feasibility studies associated with establishing an automated distributed system of national centers for the collection and storage of information on noxious chemicals.

THE INTERNATIONAL REGISTER OF POTENTIALLY TOXIC CHEMICALS (IRPTC): ITS PRESENT ACTIVITIES AND FUTURE PLANS

J.W. HUISMANS

INTRODUCTION

The deterioration of environmental quality, which began when Man first became aggregated into villages and used fire, has existed as a serious problem under the ever-increasing impacts of exponentially-increasing population and the ravages of the industrialized society.

The Middle of the Twentieth Century witnessed a rapid expansion of the chemical industry and, with it, the intrusion of chemical technology into practically all branches of the economy and into every-day life. Today, Man is synthesizing new chemicals which do not occur in Nature, and is using them in industry and agriculture as well as for medicines and a wide range of domestic purposes. Indeed, their proper use has enhanced the quality of life of millions of people.

At the same time, pollution of the environment by chemicals has resulted in serious impairment of human health and in considerable ecological and environmental damage. Some of these potential hazards to Man and his environment are recognized, but others may only appear after a considerable time lapse. It is therefore of the utmost importance that, if the hazards outweigh the benefits which chemicals bring, then their use has to be critically and objectively assessed. Many countries have passed laws and regulations regarding evaluation and control of chemicals in the environment, and require information to be submitted to national authorities before chemicals can be manufactured or used. Some of this information has been confined to certain institutions in a limited number of countries, and is not easily available to others.

The need for adequate information to assess the potential hazards posed by chemicals to Man's health and the environment has become clearly recognized very widely in the world. Further knowledge about the amounts of particular chemicals produced in the world, the pattern of their use, and their properties and effects on Man, living organisms, and the environment, as well as their distribution and transformation in the environment, is required. Improved access to information on national laws and regulations to control the use of chemicals is also necessary.

There exist, all over the world, various information systems on chemicals which are not always at all readily accessible to the experts and authorities who are responsible for regulatory decisions. Frequently the information contained in such systems is not adequately suited to the needs of decision makers. Until lately, there has been no international institution to collect and disseminate this information on a global level for all those who deal with the control of hazards posed by chemicals to human health and the environment.

IRPTC, ITS OBJECTIVES AND STRATEGIES

At the United Nations Conference on the Human Environment, held in 1972 in Stockholm, it was recommended that plans be developed for an International Register of Data on Chemicals in the Environment, based on collection of available scientific data. Following this recommendation, the Governing Council of the United Nations Environment Programme (UNEP) decided, at its Second Session in 1974, that urgent steps should be taken for the establishment of both a chemical register and an information exchange network. As a result of this decision, two meetings of experts were convened in 1975 at which guidelines, objectives, and a set of strategies for such a register were formulated.

Since its establishment as a Programme Activity Centre (PAC) of UNEP in 1976, the International Register of Potentially Toxic Chemicals (IRPTC) has been guided by the Decisions of the Governing Council and the recommendations of both those meetings. The following objectives for the IRPTC were approved by the Governing Council at its Sixth Session, in 1978:

(i) to facilitate access to existing data on the effects of chemicals on Man and his environment, and thereby contribute to a more efficient use of national and international resources that are available for the evaluation of effects of chemicals and their control;

(ii) on the basis of information in the Register, to identify the important gaps in existing knowledge on the effects of chemicals, and call attention to the need for research to fill those gaps;

(iii) to identify, or help identify, potential hazards from chemicals, and improve the awareness of such hazards;

(iv) to provide information about national, regional, and global policies, as well as regulatory measures, standards, and recommendations, for the control of potentially toxic chemicals.

To achieve these objectives, the following activities have been foreseen by the Governing Council.

A. To render the IRPTC Programme Activity Centre capable of handling data and answering questions.

B. To involve correspondents designated at the national, regional, and sectoral levels in the operations of IRPTC.

C. To build a network of participating data systems, which may make their files available to the IRPTC Programme Activity Centre for incorporation in its central data files, or may respond directly to users' queries.

D. To develop and continually update computerized central data files.

E. To publish selected information on chemicals.

The Governing Council of UNEP also requested the Member States to assist the Executive Director in establishing the network by appointing National Correspondents and to improve their national mechanisms in terms of personnel, facilities, and organization in order to enhance the capability of IRPTC to fulfil its task efficiently and effectively.

NETWORK PARTNERS

The International Register of Potentially Toxic Chemicals (IRPTC) has been designed to operate on the basis of network arrangements for information exchange, and on development of central files on chemicals which are called data profiles. From the beginning of its activities, the identification of network partners and the implementation of effective collaboration, have been priority tasks for IRPTC.

The potential partners in the network can be identified as:

(1) The Central Unit, or Programme Activity Centre (PAC);

(ii) The IRPTC National Correspondents;

(iii) Some national and international institutions; and

(iv) Industries and external contractors.

The Central Unit, assisted by a Scientific Advisory Committee and ad hoc expert consultants for special tasks, operates the network, sets the procedures for exchange of information, and communicates with countries and institutions. In accordance with the mandate given to IRPTC as a component of UNEP, it will try to improve the coordination of international activities in the field of information exchange, or to initiate new activities where there is a gap causing deficiencies and/or inadequate action. IRPTC is also actively participating within the U.N. system in implementing General Assembly Resolutions 36/166 ("Exchange of Information on Banned Hazardous Chemicals and Unsafe Pharmaceutical Products") and 37/137 ("Protection Against Products Harmful to Health and the Environment").

IRPTC assists in establishing national registers, providing special training and assistance (where necessary) to ensure effective participation of all interested national institutions and to improve understanding of IRPTC's data presentation. For this reason, a series of regional workshops was organized in 1979, 1980 and 1981, for National Correspondents of the Asia and Pacific Region, the Africa and West Asia Regions, and the Latin America Region, respectively.

In the operation of IRPTC's Central Unit, National Correspondents play an important role by providing: information on new or planned legislation to control chemicals; newly-prepared regulations and recommendations regarding chemicals; new studies on chemicals causing concern in respect to human health and

6300a

the environment; and reports on accidents and incidents involving chemicals that have led to official enquiries. They also give advice on expertise relevant to IRPTC, and distribute information processed by IRPTC.

Working relationships have also been (and are still being) established with other network partners - such as international organizations, national governmental institutions, scientific research institutes, and industry - with a common interest in chemical safety. These include, inter alia, the International Programme on Chemical Safety (IPCS), the International Occupational Safety and Health Hazard Alert System of the International Labour Office (ILO), the Joint Group of Experts on Scientific Aspects of Marine Pollution (GESAMP), the Environmental Chemicals Data and Information Network (ECDIN) of the European Economic Community, the State Committee for Science and Technology (GKNT) of the USSR, the National Toxicology Programme (NTP) of the USA, the International Group of National Associations of Manufacturers of Agrochemical Products (GIFAP), and the Japan Chemical Industry Ecology-Toxicology and Information Center (JETOC).

Several mechanisms for collaborative production of data profiles for chemicals can be envisaged, and various levels of assistance to IRPTC can be suggested. Thus there could be assistance from network partners to IRPTC in carrying out literature searches and collection of relevant documents, as well as in the preparation of data profiles for chemicals, using the machine-readable worksheets currently used by IRPTC staff.

The study and review of data profiles prepared by IRPTC could be helpful, and a possibility to compare IRPTC's chemical-ly-related sources of information with each network partner's bibliographical data base could also be most useful and mutually beneficial.

DATA PROFILES FOR CHEMICALS

The development of central files containing information adequate for an understanding of health and environmental hazards caused by toxic chemical substances, has been constantly given priority attention by IRPTC. The tentative list of attributes (characteristics) of chemicals, prepared for IRPTC in 1975, was further developed and better defined during a subsequent study which was carried out with the participation of an international group of expert consultants. This study formed the foundation for storage and retrieval of data in the IRPTC central data system, and has been initially employed in the preparation of data profiles for chemical substances. Data profiles for some 60 chemicals were prepared and published in 1979 as illustrative examples of typical IRPTC output (IRPTC - 1979)/1/. With the assistance of subcontractors, National Correspondents, and other contributing network partners (including chemical manufacturers), IRPTC staff are now preparing data profiles for approximately 450 chemicals.

The data profiles enable the expert user, worldwide, to identify what is known about a particular substance in terms of its chemical, physical, environmental, and toxicological characteristics relevant for hazard assessment. In addition, they provide information on production and consumption, use, spills, treatment of poisoning, and waste management - as well as on recommendations and legal mechanisms for control of hazards posed by chemicals. All information in a data profile is presented in extreated and condensed form together with the sources from which it was obtained. At present, an IRPTC data profile consists of seventeen attributes or files. Each of these files can be divided into subfiles, with presentation of relevant data records involving a complete item of information. The main content of an IRPTC data profile is shown in Table I.

Detailed instructions for the selection and presentation of data for the Register were developed and published in 1979 and, after recent extension and modification, they are now being widely used for data profiles development by the IRPTC Programme Activity Centre (IRPTC - 1979 and 1982) /2/. The instructions allow for uniform data input and correct description of the particular properties or effects of chemicals, as well as of any legal or regulatory information available.

Another aim of the instructions is to provide assistance to users of data profiles towards understanding fully the information contained in them. In order to provide reliable, relevant, and sufficiently detailed information to assess chemical hazards in the environment, the corresponding IRPTC files and subfiles may need further improvement regarding their content and structure. Consequently, IRPTC is continuously monitoring national and international developments in these fields.

SOURCES AND QUALITY OF DATA

The identification of all relevant sources of information on chemicals, organised in one, several, or all data fields, and the ascertaining of their quality, are necessary for the Register. The importance of the reliability of data entered into the IRPTC data bank cannot be over-emphasized, so preference is

Table I. IRPTC Data Profile Structure

1. Identifiers and Properties
2. Production/Trade
3. Production Processes
4. Use
5. Pathways into the Environment
6. Concentrations
    - Loss/Persistence
    - Concentrations
    - Human Intake
7. Environmental Fate Tests
    - Biodegradation/Biotransformation
    - Photodegradation
    - Hydrolysis
    - Sorption
    - Evaporation
    - Oxidation
    - Model Ecosystem Studies
8. Environmental Fate
9. Chemobiokinetics
    - Absorption
    - Distribution
    - Bioconcentration Factor
    - Metabolism
    - Excretion
10. Mammalian Toxicity
11. Special Toxicity Studies
    - Biochemical Interactions
    - Carcinogenicity
    - Mutagenicity
    - Neurotoxicity
    - Behaviour
    - Sensitization
    - Interacting Agents
    - Primary Irritation
    - Immunotoxicity
    - Reproduction
    - Teratogenicity
12. Effects on Organisms in the Environment
    - Aquatic Toxicity
    - Terrestrial Toxicity
13. Sampling/Preparation/Analysis
14. Spills
15. Treatment of Poisoning
16. Waste Management
17. Recommendations/Legal Mechanisms

given to information which has been evaluated by international and national groups of experts.

IRPTC has in its files a fast-growing collection of national and international criteria documents, monographs, and dossiers on chemicals, as well as nation regulations and international conventions and guidelines concerning chemicals. In cases where secondary documents containing evaluated information do not exist, IRPTC staff and network partners carefully select and review primary sources of data - always according to the instructions for the data selection and presentation. In addition, IRPTC seeks advice, as appropriate, from individual consultants, panels of experts, and international organizations.

LIST OF SELECTED CHEMICALS

Clearly, in building up an information system such as an environmental chemicals data bank, it would not be possible to consider all chemicals at once or, indeed, to devote equal attention to each of them. However, it is extremely difficult to select chemicals for priority consideration and the preparation of comprehensive data profiles. Selection criteria can be used for each chemical, such as production quantity and main uses, toxicity to Man, ecotoxicity, and persistence and bioaccumulation. Another approach for the preparation of a priority list, in fact the one followed by IRPTC, is to identify chemicals for which concern has been expressed by competent authorities at the national and/or international level. This includes lists of chemicals that are widely used, poisons, chemicals to which wide sectors of the population or workers are exposed, pesticides, etc.

In preparing an integrated list of chemicals which will gradually grow, IRPTC has tried to identify the largest possible number of chemicals of international significance. The IRPTC Working List of Selected Chemical Substances at present includes approximately 450 chemicals, of which 160 are agrochemicals; but it is by definition open-ended, and will undergo considerable expansion on the basis of proposals made by National Correspondents, the International Programme on Chemical Safety, and IRPTC network partners.

LEGAL DATA PROFILES FOR CHEMICALS

On several occasions during sessions of the Governing Council of UNEP and the General Assembly of the UN, as well as at other international forums, concern has been expressed about the possible serious adverse effects of the increasing number of chemicals entering the environment. Information exchange among governments on chemicals and their likely effects and measures taken to eliminate or control such effects was considered to be of prime importance. International organizations were requested to assist governments in establishing information exchange procedures. The Governing Council of UNEP, in its Decision 6/3 B (1978) requested that priority be given to providing countries with information on legal and administrative limitations, bans and regulations placed on potentially toxic chemicals in the producing countries. Moreover, the General Assembly of the UN, in its Resolution 37/137 (1982) and previous Resolutions on the same subject, requested the preparation of a list of products (including chemicals) whose consumption and/or sale have been banned, withdrawn, or severely restricted by governments.

In response to these requests legal data profiles containing data on "Recommendations/Legal Mechanisms" (one of the 17 broad groups of attributes mentioned above) are being developed as a priority, although they form part of the data profile series. National (eight selected countries) and international recommendations and regulations for the control of about 200 chemicals in air, water, wastes, soil, food, beverages and consumer goods were collected and published (IRPTC: Data Profile Series Number Two - Legal Data Profiles for Selected Chemicals, 1980) /3/. The chemicals were selected from the IRPTC Working List of Selected Chemical Substances based on existing national and international lists. The updated and expanded IRPTC legal data file, which now contains data on approximately 450 chemicals from 12 countries and 6 International Organizations, will be published in 1983. Further updates including more chemicals are planned for the future and will be published at regular intervals.

USERS AND QUERY-RESPONSE SERVICE

The most important user group of IRPTC is represented by national authorities that are responsible for protection of human health and the environment. Decisions to regulate or control chemicals must be based on 'best-informed' judgement. IRPTC aims at providing its readers with a reliable, up-to-date and comprehensive presentation of information necessary to assess the risk caused by chemicals to Man and his environment.

The scientists involved in experimental research can hardly expect from a computerized data bank such as that of IRPTC the detailed information that would obviate for them the necessity of reading the original sources of data. However, they can use the Register to identify priority chemical substances which may have the potential for being hazardous, and on which little or no pertinent research has been performed to elucidate this potential. International bodies, such as the International Programme on Chemical Safety, could use information from the Register as a basis for production of evaluation documents, as well as for identification of gaps in knowledge and for the planning of future studies.

Information contained in the Register is also of interest to both government and industry in the development of guidelines and recommendations on chemicals control, or in the determination of likely effects when planning chemical research.

A Query-Response Service is now in operation and provides, on request, information on specific chemicals. Questions may be answered by the Central Unit, using information contained in its data profiles and library system, through searches of on-line data bases, or with the assistance of partners in the network when relevant information is not available in the Register. Other international bodies or expert consultants may help in answering questions.

DATA MANAGEMENT AND IRPTC PUBLICATIONS

Growth of documentation received from many sources necessitates optimal access to the relevant data which it contains. Also, data profiles have to be processed and stored in a computer, using an adequate software package allowing easy updating and retrieval of information. The terminals now in use in the IRPTC Central Unit are connected to the International Computing Centre (ICC), Geneva. Access to relevant on-line information systems has been established.

Having reached the stage of computerization of the data compiled on chemicals, and taking into consideration several criteria, IRPTC has decided to implement its information bank through the Data Base Management System 'ADABAS' which is now being adapted to provide the services required by the Register.

Some data bases have already been organized and stored. Foremost among these is the Register Index, published every four months, which consists of the IRPTC Working List of Selected Chemical Substances, accompanied by pointers showing on which data fields IRPTC has information in its files. Another important data base contains the IRPTC library records. Over 3,000 publications have been indexed up to now, according to a format and a thesaurus developed by IRPTC.

In addition to production of data profiles, IRPTC also publishes a BULLETIN which contains information on IRPTC activities, other activities of UNEP, international and national organizations related to chemical safety, but the main emphasis is on current intelligence information on chemicals. This includes information on new or proposed legislation and regulations for the control of chemicals in the various environmental media, international risk evaluations, newly-discovered hazards, accident reports and safe use instructions for chemicals. National Correspondents actively participate in providing information for the BULLETIN and distributing it within their respective countries. Other network partners also provide new information for inclusion in the BULLETIN which is published in four languages (English, French, Russian and Spanish) and issued three times a year to over 8,000 addresses. A joint project with the Centre of International

Projects of the Commission for UNEP, State Committee for Science and Technology of the USSR, provides for, inter alia, Scientific Reviews of Soviet Literature on Toxicity and Hazards of Chemicals and other scientific publications and monographs related to chemical safety as well as training courses and meetings on specific topics.

Further scientific publications and data compilations are foreseen in the near future.

REFERENCES

1. 'Instructions for the Selection and Presentation of Data for the International Register of Potentially Toxic Chemicals with Sixty Illustrative Chemical Data Profiles' (IRPTC Register Attribute Series Number Two - 1979).

2. Ibid and 'The International Register of Potentially Toxic Chemicals - Part A' (1982).

3. 'Legal Data Profiles for Selected Chemicals' (IRPTC Data Profile Series Number Two - 1980).

THE INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY (IPCS)

M.Mercier, M.Gounar

In 1977, the World Health Assembly, concerned about the enormous developments in the use of chemicals in a wide range of human activities, and recognizing the inadequacy of existing national and international efforts to deal with the long-term aspects of human exposure to potentially dangerous chemicals, requested the Director-General of the World Health Organization (WHO) to study the problem of long-term strategies to control and limit the impact of chemicals on human health and the environment.

The problem clearly has international dimensions, not only because of the international trade in chemicals, but also because a collaborative approach is needed for a sound and thorough evaluation of their effects. Moreover, an international collaborative approach is the only way to avoid costly duplication of national efforts to test and assess chemicals, and to put our scarce and valuable resources in toxicological expertise to the best possible use.

Moreover, because of the many activities, principally among the more technologically advanced nations, concerning the control of toxic chemicals, it became clear that, unless a concerned and collaborative effort was made, many governments, particularly those from the developing world, could fall further and further behind in the development of both the means and the expertise to tackle the increasingly complex health and environmental problems caused by the use of chemicals.

The World Health Assembly therefore invited the Director-General to examine, in collaboration with appropriate national institutions and international organisations, the possible options for international cooperation, including the financial and organizational implications, bearing in mind the activities being carried out by the International Agency for Research on Cancer (IARC) and the UNEP International Register of Potentially Toxic Chemicals (IRPTC). The Executive Board, at its 1979 session, endorsed the Director-General's proposed content, structure and measures for implementation of the International Programme on Chemical Safety (IPCS) which, after its endorsement by the WHA, came into being in 1980, though the establishment of a Central Unit (CU) at WHO Headquarters in Geneva, to plan and coordinate the work which is carried out by a network of national and international institutions.

Although the IPCS was initially conceived as a WHO activity, it has now become a cooperative venture of the International Labour Organisation (ILO), the United Nations Environment Programme (UNEP), and WHO.

Objectives of the IPCS

The present and future objectives of the IPCS can be summarized as following:

1. to carry out and disseminate evaluations of the effects of chemicals on human health and on the quality of the environment;
2. to develop guiding principles on exposure limits (such as acceptable daily intakes, and maximum permissible or de-

sirable levels in air, water, food and the working environment), for several classes of chemicals including household products, contaminants, cosmetics, food additives, industrial chemicals, toxic substances of natural origin, plastics, packaging materials, and pesticides;

3. to encourage the use and improvement, and in some cases, the validation of methods that could produce internationally comparable results, particularly as regards methods for exposure measurement and assessment, toxicity testing, epidemiological studies, and risk assessment and hazard evaluation;
4. to coordinate laboratory testing and epidemiological studies, when an international approach is appropriate, and to promote research in those areas;
5. to develop know-how for coping with chemical accidents, and to promote effective international cooperation in this field;
6. to promote technical cooperation with respect to specific issues concerning control of toxic substances in Member States;
7. to promote training and development of manpower in the field of toxicology.

These are indisputably ambitious objectives, but it must be emphasised that the IPCS is not an entirely <u>de novo</u> activity. The 3 Cooperating Organisations (COs), i.e. UNEP, ILO and WHO, have already a distinguished record of results in evaluating the safety of chemicals; the IPCS aims at strengthening the existing activities and initiating new ones.

To achieve these objectives, the necessary resources, financial and human, are provided by the Member States of the

COs. The response so far is encouraging, 15 countries having provided very substantial voluntary contributions to the Programme.

Structure of IPCS

The following elements make up the organizational structure of the IPCS.

1. The Central Unit (CU) is responsible for the overall management, cohesion and implementation of the programme on behalf of the cooperating organizations.

   Its main functions are:

   a. to develop plans and programmes of work;

   b. to coordinate the programme components located at national and other Lead Institutions (LIs) and at Regional Offices, and to ensure liaison with other international organizations;

   c. to provide technical and scientific support for the programme.

The Inter-regional Research Units (IRRUs) are extended areas of the CU which operate under the general direction of the Manager, CU and assume the responsibility for the planning, development and implementation of specific projects and activities and maintain liaison with national collaborating institutions. The first established IRRU is located at the National Institute of Environmental Health Sciences (NIEHS) in the United States.

2. The Inter-Secretariat Coordinating Committee (ICC) comprising representatives of the Executive Heads of the COs, reviews and decides on proposals and workplans for IPCS. It

also advises on, and keeps under review, the staffing of the CU and the IRRUs.

3. The Programme Advisory Committee (PAC) consists of 20 members appointed by the Director-General of WHO in consultation with the Executive Heads of the other COs. It advises the Executive Heads of the COs on policy matters and in setting the overall goals and global priorities of the programme.

4. The Technical Committee (TC) consists of the directors of the LIs and is the operative organ with multidisciplinary scientific and technical capacity. The TC prepares the annual workplans and sets operational priorities in order to achieve the policy goals set by the PAC.

5. The Lead and Participating Institutions (LIs and PIs) The working mechanism of the IPCS is a net work of LIs and Participating Institutions (PIs), designed to achieve an organized distribution of work among the countries actively participating in the IPCS. The LIs are designated by the Executive Heads of the 3 COs after negotiation with the respective governments, to ensure that IPCS commitments are met, and that support (including sufficient national staff) is provided. In designating an LI, internationally recognized competence in a specific field is the criterion of choice. At present, there are 20 LIs located in 14 different countries. Subnetworks, made up of PIs and designed for specific programme areas, are established to work with the LIs and are guided and coordinated by the LIs.

6. The International Lead Institutions

Two international LIs have been designated. The International Agency for Research on Cancer (IARC) is the LI for chemical carcinogenesis. The International Register of Toxic Chemicals (IRPTC) of UNEP is operating as LI for the collection, retrieval and dissemination of information.

7. International, Inter-Country and Non-Governmental Organizations (NGOs)

The IPCS is cooperating with a number of international and inter-country organizations, including the Food and Agriculture Organization (FAO), the Commission of the European Communities (CEC), the Council for Mutual Economic Assistance (CMEA) and the Organization for Economic Cooperation and Development (OECD).

Close cooperation has also been established with non-governmental organizations actively working in the field such as the Monitoring and Assessment Research Centre (MARC), the Scientific Group on Methodologies for the Safety Evaluation of Chemicals (SGOMSEC), the European Chemical Industry, Ecology and Toxicology Centre (ECETOC), the International Commission for Protection Against Environmental Mutagens and Carcinogens (ICPEMC), the International Petroleum Industry Environmental Conservation Association (IPIECA), the International Brain Research Organization (IBRO), the Association of Plastic Manufacturers of Europe (APME), the World Federation of Associations of Clinical Toxicology Centers and Poison Control Centers, the Toxicology Forum, the Chemical Industry Institute of Toxicology (CIIT), the International Life Science Institute (ILSI), etc.

The Work of the IPCS

The responsibilities envisaged for the IPCS in the field of chemical safety are extensive and far-reaching and it will obviously take time to develop the necessary integrated programmes and obtain the level of support to make a significant contribution to this challenging global issue. It was recognized that there were many activities, both in WHO and other United Nations organizations, that were relevant to some aspects of chemical safety and that, thus, there was a need for the IPCS to be concerned with liaison and coordination efforts. Some existing activities could be incorporated into the IPCS. The most important of these were the WHO side of the joint efforts of WHO and FAO in the areas of food additives and pesticide contamination and the WHO/UNEP environmental health criteria programme. To these have been added in the first phase of the development of the IPCS programme, two new activities: the first is the promotion of new developments in methodologies for the detection and study of the health effects of chemicals, the second the adaptation, for international needs of the various guidelines currently in use, or proposed, for testing the toxic properties for legislative purposes. The WHO Regional Office for Europe (EURO) has undertaken important work in the area of manpower development in toxic chemicals control and response to emergencies resulting from major accidents involving chemicals; EURO is now assuring a lead role with regard to those two activities within the framework of the IPCS.

1. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the Joint FAO/WHO Meeting on Pesticide Residues (JMPR)

JECFA was first convened in 1956 following the initiative of the 6th World Health Assembly in 1953. At that time, concern was expressed that the increasing use of various chemical substances by the food industry during the past few decades had created a new public health problem that might usefully be investigated. It was subsequently recommended by the WHO Executive Board that, in cooperation with FAO, information should be collected and disseminated on selected groups of chemical additives used in food including testing techniques and relevant legislation. Following this, in 1963, in a somewhat similar manner, the problem of toxicologically evaluating pesticide residues in food was dealt with by setting up a Joint FAO/WHO Meeting on Pesticide Residues (JMPR). Both bodies have produced a large number of reports and monographs of great value to the responsible authorities in the Member States. Of considerable importance for the regulatory authorities is the development of the concept of an acceptable daily intake (ADI) within the toxicological evaluation of the food additives. The ADI provides an indication of safety in the use of the food additives in question and enables authorities to take adequate legislative measures for their control. In considering contaminants such as heavy metals, the JECFA established a further important concept - that of the provisional tolerable weekly intake.

2. The Environmental Health Criteria

The purpose of these criteria is to summarize, review, and evaluate the available information on the effects of a specific chemical or a group of chemicals that may influence human health and the environment, and to provide a scientific basis for policy decisions aimed at protecting human health and the environment from the adverse consequences of exposure to such chemicals. The production of such authoritative documents, is a careful and meticulous process, the final risk evaluation being made by a task group of independent international experts covering a wide spectrum of aspects of the subject, relevant to human health and the environment.

In addition to these documents, a series of short documents is planned so that important information can be made available to those responsible for chemical safety with a minimum of delay. In this work, the IPCS will be collaborating not only with Lead Institutions but with UNEP's International Register of Potentially Toxic Chemicals (IRPTC).

3. Improvement of Methods for the Detection of Health Effects of Chemicals and the Assessment of Health Risks

This third component of the IPCS is concerned with efforts to encourage the development of reliable methods for detecting the toxic properties of chemicals, particularly in relation to effects that may not be manifest for months, years, or even generations.

Monographs on Principles and Methods for Evaluating the toxicity of Chemicals and on Guidelines or studies in environmental epidemiology are already published or in an advanced stage of preparation.

For several selected areas, special working groups have been established with the tasks of reviewing in detail the present methods and their predictive value, identifying the needs for cooperative methods, assisting in the coordination of these studies, and finally, serving as more permanent advisory bodies on the relevant problems with the IPCS. Several working groups have commenced their work dealing with important fields such as the assessment of genotoxicity, reproductive toxicology, neurotoxicity, particularly neuro-behavioural toxicity, immunotoxicology and on the effects of chemicals on the cardiovascular and endocrine system. Other topics of interest include the methodology of assessing the effects of multiple exposure to chemicals the extrapolation of experimental data to effects on human subjects and the qualitative estimation of risk to human health from chemicals.

However, it is not only essential to develop new methods in testing, but that it is also necessary to consolidate methods already generally agreed to be useful. A number of national and international agencies from the industrialized nations have developed principles of good laboratory practice and guidelines for the testing of chemicals for a number of important toxic properties. The problem is how these procedures and their consequences should be made known to the less developed parts of the world. The adaptation and dissemination of such guidelines for the information of, and possible use by, health authorities and others in countries that lack expertise in these matter is a high priority objective of the IPCS.

4. Manpower Development in the Field of Toxic Chemicals Control

The capacity of most countries, especially the developing ones, to regulate the safe use of chemicals or to adapt to the country the results of risk evaluation made elsewhere has been largely limited by a shortage of appropriate experts.

IPCS has therefore given high priority to manpower training and has developed a programme which includes:

1. Compilation of occupational profiles with a basic forecast of the needs in the various categories.
2. Analysis of existing national training programmes and development of complementary curricula.
3. Development of manuals and other teaching aids for training activities in toxicological expertise.
4. Organization of workshops, training courses and seminars adapted to the needs of the Member States.

The WHO Regional office for Europe (EURO) is assuming a major role on behalf of the IPCS for that component.

5. Management of Chemical Emergencies

Finally any programme on toxic chemicals control must deal with the ever present possibility, indeed tragic reality, that, in the daily production, transport, storage, use and disposal of millions of tons of chemicals, accidents will occur and some of these accidents will involve the release of dangerous materials into the environment. Such release may have extremely serious consequences. Within the frame of the IPCS, the European Regional Office of WHO is developing systems and strategies for managing chemical emergencies, so that the combined resources of local, national and international services can be coordinated for an appropriate response.

A more stringent evaluation of the chemicals to which we are exposed is needed by all Member States, and there is no doubt that, for countries unable to make such evaluations, an international assessment is more acceptable than one carried out by another national authority. Consistency in testing will facilitate comparability and acceptance of the data obtained in different countries, and will promote both international trade in chemicals and the standardization of control measures.

The increase in the number of accidents involving toxic chemicals makes it imperative to share our expertise and experience, and the IPCS provides an international infrastructure for doing so.

6. Participation of Developing Countries in the International Programme on Chemical Safety*

The IPCS feel that a specific component within the Programme's activities should be devoted to the needs of the developing countries. And there are a lot of reasons for that. Some of them are the following:

- About seventy percent of the world's population lives in developing countries. The large human populations living in these countries are subject to risks of exposure to chemicals similar to or even higher than population in developed countries.
- Illiteracy, endemic diseases and exposure to environmental chemicals are common in developing countries. On the other hand, atomic energy plants and sophisticated research centres are also found in several developing countries. It should be emphasized that all developing countries are not alike either in the stage of development or in the availability of natural resources. Some of them are well developed in certain areas while others are in an early stage of development in all areas.

---

* Based on Working Paper for an IPCS Consultation, Kiev, 23 June 1982, held in conjunction with the 3rd Session of the IPCS Programme Advisory Committee, Kiev, 23-28 June 1982.

The availability of natural resources in some developing countries helps in their rapid economic development (including their chemical industry) with adequate attention being paid to the preservation of health and environment. Most of the developing countries are in the hot and humid tropics and their economy is mostly dependent on agriculture. As a result, they have to use large quantities of agricultural chemicals including pesticides. But these chemicals are often used indiscriminately. Very often these countries do not know where and what kind of chemical substances are in their environment. In consequence, the degree and extent of exposure of the population to chemicals of not known.

Several developing countries are also becoming a dumping ground for highly toxic and pollutant substances and wastes produced in developed countries. Hazardous chemicals which are not sold in the country of manufacture because of stringent national legislation are nevertheless exported to developing countries which do not have such protective legislation. During the last three years, the UN General Assembly has noted this practice with regret and has urged Member States to exchange information on hazardous chemicals and urged them to discourage such export. Evaluated information on safe use of chemical substances is frequently not available.

Unfortunately, most of the information received from international organizations by the contact point in the country is not reproduced and distributed to the responsible persons and institutions in the country.

Many developing countries do not have appropriate regulatory and control measures for toxic chemicals. This has led to indiscriminate manufacture, import, transport and use of these chemicals resulting in 'unknown' exposure to them.

And finally, the capacity of developing countries to regulate the safe use of chemicals or to adapt to the country the results of risk evaluations made elsewhere has been limited mainly by: a) shortage of appropriate experts and institutions; b) decision makers not sensitive to these problems; c) pressure exerted by commercial firms and interested industries.

However, despite these shortcomings, there is a good potential in some institutions in developing countries. With the experts and facilities available, these institutions could form a nucleus to participate actively in the International Programme on Chemical Safety.

By now a few developing countries, India, Brasil, etc., are already deeply involved in activities similar to those of the IPCS indicating that the concern about the impact of chemicals on the human health and environment is not confined to the developed countries.

At present, WHO provides assistance and/or information on request from Member States; however, some decision makers do not often realize the importance of chemical safety and environment protection and are unable to identify the exposure of the population to hazardous chemicals. Often these decision makers are not aware of the environmental health problems caused by chemicals; sometimes their attention is diverted from these problems by the literature supplied by commercial firms and manufacturers. Decision makers therefore should be made aware of the assistance which IPCS could give them in the form of evaluated information on chemicals.

I would like to underline, that the Regional Offices of WHO which have long experience and expertise should be more actively involved in IPCS by providing assistance:

(1) for the co-ordination of IPCS activities both with countries and within the region and

(2) for the periodical visits of IPCS staff and consultants in the region.

Scientific institutions and universities in developing countries possessing the necessary facilities and experties to undertake various aspects of IPCS are being identified now. Once they have been identified and specific task assigned to them, scientists in other developing countries themselves. Some of these institutions and universities could in course of time be upgraded into regional or subregional laboratories with assistance from IPCS. When necessary, the Central Unit would provide resources for the institutions in developing countries to carry out their tasks in IPCS, including manpower training and development.

It should be emphasized that chemicals pervade all elements of man's environment and affect his health and environment. Therefore, the steps taken to ameliorate their effects in the developing countries have to be taken in conjunction with the primary health care programme of WHO with the overall objective of Health for all by 2000.

HAZARDOUS EFFECT OF PARTICULATES AND CHEMICALS ON HUMAN ORGANISM AND METHODS OF THE STUDY OF PARTICULATE AND FIBROUS INDUSTRIAL TOXICANTS

S.H.Zaidi

Man has been exposed to particulates and chemicals since antiquity when work place operations were the same all over the world.

This is the inside of Ajanta Temple in India executed out of one solid granite rock. This one-piece sculpture-temple is the world's greatest rock poem. The monks and the stone-cutters who worked here and inhaled dust broke down and died young. Verses and Legends tell the story quote "the lives are almost a constant round of painful toil, their almost naked body is quickly broken down and they commonly die at the age of 35 and 40 years". And at the same time in Europe, Hippocrates emphasized the study of pollution of environment, nature of winds, hot or cold and their influence on health.

Today in the developing world rapid industrial and technological advancement is in many ways a contrast to the pattern of industrial development which occurred in highly industrialised countries where there was a gradual transformation from agrarian to industrial environment. Industrialisation has brought infinite benefits to us but is also giving rise to a host of problems and one of the major problems is pollution.

There are two kinds of substances which are directly or indirectly responsible for pollution. The first category includes the substances that already exist in nature. The second category is the whole range of new man made substances like polymers, synthetic chemicals, over 9000 in number which enter the biosphere through deliberate or careless action. There is a ready-made laboratory in nature to deal with the first category of substances. As for the second category, the problem is very complex.

The chemicals that cause pollution can be in the form of gases and particulate material.

The term 'gas' is usually applied to any material that is in the gaseous state at 35°C and 760 mm of mercury, while 'vapour' is the gaseous phase of the substance which is liquid or solid at 25°C and 760 mm mercury. The distinction between the two is not sharp, for example, hydrogen cyanide, which boils at 26°C, is referred to as gas, but hydrogen chloride, which boils at 83.7°C, is often referred to as an acid vapour.

Particulate matter may be in the form of aerosol which is dispersion of solid or liquid particles of microscopic size in a gaseous medium. The examples are the smoke, fog and mist. Smoke has particles from incomplete combusion predominantly carbon. Fog is visible aerosol in which the dispersed phase is liquid.

Solid particles generated by condensation from the gaseous state accompanied by chemical reaction such as oxidation are fumes.

These chemicals may enter the human system through inhalation, injection or through skin absorption.

SKIN ABSORPTION

Contact dermatitis is known since the time of Celsus who described it in his book De Re Medicina. Today primary irritant contact dermatitis occurs in 70% of all occupational dermatoses. It is due to direct action of irritants on exposed surface of the skin. There is acute erythema, oedema, papules and vesicles, bullae, crusting and scaling of tissues. Less common are neoplastic indolent ulcers, pigment changes and hair loss.

Cutaneous response to irritants is dependent on strength and length of contact of irritant. Strong acids produce albumates and this effect resembles a thermal injury. Strong alkalis combine with fats and dissolve keratin. Metallic salts of As, Hg, Cr, combine with skin proteins and cause ulceration. Acne formation occurs by chlorinated naphthylenes and cutting oils. Carcinogen if present in irritants produce tumours.

Alergic dermatitis constitutes 15-20% of all occupational dermatoses. Response to allergen is delayed for week or more. It is usually due to one agent. Eczema is a delayed type of hypersensitivity reaction. Common sensitising agents are aniline derivatives, antibiotics, dyes, paints, inks, cosmetics, metals like As, Cr, Ni, Co, resins epoxy and formaldehyde resins, venyls and acrylics. Rubber chemical accelerators, vulcanizers and anti-oxidants, plants like daffodil, chrysanthemum, tulip, trees like African mahogany, iroko, red cedar and pharmaceuticals like procaines, tolbutamide cause allergic dermatitis.

Physical agents may cause frictional dermatitis.

Cutaneous manifestation of systemic poisoning are with As, Pb, Cr. Ag, aniline, dinitrophenol and alopecia due to As or thallium, may be noted.

Skin tumours were first described 200 years ago by Pott who observed that Chimney Sweepers had scrotal cancer. Shaleoil workers, mule spinners and other occupational group who came in contact with mineral oil develop pre-malignant papilloma or frank squamous cell carcinoma. Ultra -violet radiation may cause tumours, radioisotope handlers may also develop squamous cell carcinoma. Arsenic and arsenical also cause the growth of epethelioma in exposed workers. Prognosis of skin cancer is better than for many other sites.

THE NERVOUS SYSTEM

The toxic action of a chemical to nervous system may be peripheral or central. In toxic peripheral neuropathy, both the motor and sensory functions are affected. Glove and Stocking type of sensory loss and para-aesthesia is seen. There is symmetrical muscle weakness and wasting. Axon are usually affected more than Schwann cells. If exposure stops the nerve fibres may regenerate.

Chemicals which induced behavioural changes are CO, CS_2, inorganic mercury, Halothane, methylene chloride, Trichlorethylene, toluene methyl chloroform, styrene and white spirit.

Other side effects of chemicals on CNS are Parkinson like syndromes.

Toxic organic psychosis is the result of toxic damage to brain. There is disruption of normal brain function. The symptoms are constant. The patient develops ideas of dellusion reference persecution, memory is impaired and hallucinations occur. Chemicals which produce toxic psychosis are As, Pb, Mn, Hg, CS_2.

In this country it has long been the practice to establish hygiene standards on the basis of behavioural changes. This study has been done since the time of Pavlov.

Conduction velocity is impaired and in severe demyelinating neuropathies it may be slow by 30%. Some workers may not show overt signs or symptoms but may have electro-physiological abnormalities in the form of slowing of motor conduction velocity like in Pb workers.

Some of the chemical that cause peripheral neuropathy are Triorthocresyl phosphate (TOCP), acrylamide, CS_2, Hg compounds both inorganic and organic, diethyl thiocarbamate, n-hexane, methyl, butyl ketone, As, inorganic lead, thallium and antimony.

CARDIOVASCULAR SYSTEM

In recent years there is evidence that environmental pollution or work exposure may lead to involvement of cardiovascular system and some metals and organic compounds have been associated with it. Pb has been attributed to cause cardiomyopathy, nephropathy and hypertension. As smelting has a higher risk to heart disease than general population, Cd causes Corpulmonale and Cobalt Cardiomyopathy. Other metals linked with heart disease are Antimony, Chromium, Mn, Hg, Niobium, Vanadium and Zirconium.

Among organic compounds, Nitroglycerene and Nitroglycol workers have shown higher mortality from acute myocardial infarction than normal population, although nitroglycerene in therapeutic doses is used for angina pectoris. CS_2 causes atheroma is well established. Organochlorine pesticides like chlordane and hepatochlor have been linked with childhood tumours.

BLOOD

Red cell damage can occur by chemicals which may be trivial or severe leading to death. Most chemicals act at one stage of maturation but some act on more than one stage of maturation like lead. Bone marrow damage is reported and aplastic anaemia occurs with benzene trinitrotoluene (TNT) and irradiation. Last known exposure is usually about 10 years.

Apparatus devised by Polley (1963) for dust inhalation experiments is in use in several pneumoconiosis research centres in Europe. It consists of an animal chamber with canals in which the charge of air can be controlled to 0.3 meter/sec. The dust is generated by two dust generators and the cloud measured by Tyndalloscope.

ROCHESTER GAS CHAMBER has a pyramidal top and bottom made of stainless steel and slide of polymethyl methacrylite. It has been used in States for the last 25 years and during this time it has undergone various modifications. It is used both for gases and particulate matter. It can accommodate 16 monkeys, 32 beagles or 160 rats.

There are other simpler and quick methods besides dust inhalation chambers for the study of toxicity of dusts and fibres. Intratracheal injection, intrapleural, intracutaneous, sub-cutaneous, intra-popliteal, anterior chamber of eye-intravenous, Mecaness chamber, RBC haemolysis, Roswell method, Selye Pouch method.

For the study of the pathogenicity of asbestos fibres, intrapleural injection of dust is also used. Wright (1974) has described a three way syringe for such injections.

The study of the toxicity of dust requires a proper choice of animal, the knowledge of the nature of dust, mode of administration, quantity and period of administration to the animal. Species specificity exists. There are genetic differences minor variations in the anatomy of pulmonary tissue as well as endocrine influences and enzymatic differences.

The reaction of dust in different species under similar experimental conditions also show variations. For example, silicotic nodules in guinea pigs and rabbits are not compact as in the human, but in the albino rats there is compact nodule formation similar to that seen in man.

There is a close relationship between animal experiments and epidemiology. This relationship has provided a useful hypothesis to design not only epidemiological survey but also appropriate animal experimentation in relation to occupational diseases.

EXTRAPOLATION OF DATA FROM ANIMAL EXPERIMENTS AND EPIDEMIOLOGY

There has been discovery of industrial carcinogens after epidemiological survey. Some of them are:

COAL TAR
CREOSOTE
MINERAL OILS
RESIDUES OF PETROLEUM
IONIZING RADIATIONS
BURNS
SOOT
AROMATIC AMINES
PETROLEUM WAXES
TOBACCO
ULTRAVIOLET RAYS
HEAVY METALS AND ASBESTOS

EXTRAPOLATION OF DATA FROM ANIMAL EXPERIMENTS AND EPIDEMIOLOGY

There has also been discovery of industrial carcinogen after animal experimentation.

4-AMINO-BI-PHENYL
AFLATOXINS
DIETHYL-STILBESTROL
BIS CHLOR-O-METHYL ETHER
VINYL CHLORIDE
MUSTARD GAS
ACET AMIDO FLUORENE
CHROMIUM PIGMENTS

Toxic effects are modulated by geography, race, age, sex, nutrition, immunity status, infections, degenerative diseases and overall interaction of the macro-environment with the micro-environment. These factors should, therefore, be taken into consideration when results of epidemiological studies are being correlated or extrapolated with the data obtained by animal experiments. The best example of the close relationship between animal experiments and epidemiology has been studied in relation to cancer in asbestosis.

ASBESTOSIS AND CANCER

Toxicological Methods	Epidemiological Methods
Proof of Causation	Proof of Association
Effect of Pure Exposures	Estimates Excess Risks
Importance of Size, Shape and Composition of Fibres	Dose Response Relationship

Assessment
of
Future Risks

Today, in industry asbestos is a mineral of a thousand uses, from heat resistance to clothing and brake lining. It is now established that asbestos dust is harmful per se and causes a high morbidity and mortality. Recently chemical, physio-chemical and biological properties of asbestos have been reviewed by Synder and pathology described by Meyer.

Regarding pathogenesis of asbestosis typical are asbestos bodies. The formation of asbestos bodies has been reviewed by Das and his colleagues.

It is now possible to characterise and differentiate asbestos fibres from other bodies by electron micro-probe analysis.

In cases of asbestosis plaques are seen in pleura. This thickening of pleura which often gets calcified and occasionally hayalinised has been attributed to asbestos inhalation or previous pleural disease.

For increase in lung cancer among asbestos workers, predisposing factors have been suggested which are inheritance race and co-factors like cigarette smoking. All these are under investigation.

Harington demonstrated that tumours developed both with untreated asbestos and with the samples from which hydrocarbons were extracted and Cralley suggested that trace metal are cause of lung cancer in rats. The importance of waxes and oils or trace elements in the production of mesotheliomа have not received support.

According to Gross lung cancer develops only in those asbestos workers who are heavily exposed to this dust.

Regarding Gastrointestinal and Laryngeal tumours: Asbestos has been suspected to cause an increase in the incidence of tumours. A relationship between smoking and laryngeal cancer caused by dust inhalation has been described.

Wagner et al. reported mesothelioma in asbestos workers. It occurs with crocidolite variety or to a mixture of different varieties of asbestos dusts. Only a few fatal cases in amosite and none in anthophillite mining have been reported.

RISK ASSESSMENT AND THE MANAGEMENT OF TOXIC CHEMICALS

Côté R.P.

INTRODUCTION

You have now had two months of toxicology, some of it very general, some of it very detailed information. And while toxicology data are extremely important in making decisions about the use, transport or disposal of a particular chemical, those data are only one of several factors which must be considered.

The decisions I am referring to include:

i) total prohibition.
ii) limited use within set standards
iii) use with compensation
iv) unlimited use

And if toxicology information is not the only basis for making such decisions, what are the other kinds of information?

a) transport and fate of the chemical
b) availability of control alternatives
c) the economics
d) legislative tools and legal remedies
e) the perceptions of various publics

I have been asked to speak to you primarily about the industrial environment, the workplace. I have purposefully chosen to use a broad definition which encompasses the importation or extraction, transportation, processing or manufacture, the end use and the disposal, all of which have an industrial or occupational component. It is only by thinking broadly that we are going to


POISON

manage toxic chemicals thereby ensuring that we get maximum benefits and minimum costs. What I want to do is to put toxicology and then risk assessment into a context, a decision-making context.

THE SCOPE OF THE PROBLEM

I'd like to begin by reminding you of the major industrial sources of chemicals. They are:

Pulp and paper
Base metal mining and smelting
Wood preserving
Metal plating
Steel manufacturing
Petroleum refinering
Tire manufacturing
Coal mining
Textiles
Petrochemical industries
Pesticide manufacturing
Thermal electricity generating
Shipping
Offshore exploration
Agriculture

In other words, just about every industrial activity uses or releases chemicals. And while we seem to be continually surprised by findings that chemical "X" causes cancer or chemical "Y" causes liver damage, history is replete with examples. The hazards of asbestos were known as early as 1 A.D. in the Roman Empire; chimney sweeps in England developed scrotal cancer in the late 1700's; workers in the felt hat industry developed "Mad Hatters" syndrome in the 1800's and German workers in aniline dye manufacturing plants were linked to bladder cancer around 1895. And we can add a large number of more recent events involving kepone, polyurethane foam, lead, dibromo chloropropane, 2,3,7,8, tetrachloro dibenzo-p-dioxin and benzene. That there are events of serious consequences associated with the many elements of the industrial environment is further exemplified by such unlikely but credible accidents as:

- Destruction of factories and their neighbourhoods in Cleveland, U.S. in 1944 resulting from an LNG tank failure or the dioxin release in Seveso, Italy, in 1976.
- Injury or death to hundreds of people along the transportation route of vehicles carrying highly toxic or flammable compressed gases as occurred near the Las Alfaques campground in Spain in 1978 involving a propylene tanker accident and fire.
- Injury or death to people or animals, one or a few at a time, because of a defect or contamination of a product as for example, the poor location and protection of fuel tanks of certain car models resulting in frequent fires during rear collision and polybrominated biphenyls in cattle feed resulting in the destruction of several thousand cattle in Michigan, U.S. Minimata disease in Japan is another good example.

HAZARD IDENTIFICATION

By making an inventory of the sources, you have begun a process of identifying the hazards.

I will define hazard as a statement which addresses the inherent toxicological properties of a chemical and knowledge of its transport and transformation properties. Dictionaries define it as a source of danger. Some authors such as Somers (1980); Whyte and Burton (1980) refer to this as risk identification.

The toxicity of a compound can be determined in several ways. Where time is of the essence, a qualitative structure-activity relationship could be developed with compounds known to be of similar composition and structure. Another commonly used method is the 96 hour bioassay with rainbow trout, Salmo gairdneri or the bluegill sunfish Lepomis macrochirus.

The information derived here cannot be considered as definitive and could lead one to erroneous conclusions without additional evaluation. As examples, I have only to mention that 2,3,7,8 TCDD is more toxic than either the trichloro or pentachloro isomers. Also a-napthylamine is not carcinogenic while b-napthylamine has been shown to be.

On the other hand, where the chemical is used extensively and transported widely, a full series of tests can be implemented to provide reasonably conclusive data. I used the word reasonably conclusive because there is no absolute safety. Such a series has been called a tiered hazard evaluation and involves;

1. Screening studies such as acute toxicity tests use one to three species preferably at different trophic levels or in different media. These are generally of short duration and involve minimum expense.
2. Predictive tests of a chronic nature which could involve studies over one or two generations with additional testing for carcinogenicity, teratogenicity, skin sensitiza-

tion and neurologic damage. These tests are more rigorous but require a greater involvement of time and money.

3. Confirmative tests often involving field studies or microcosm studies which are used to confirm some of the laboratory data generated. Such tests will also enable the investigator to assess the ecotoxicological implications of the chemical.
4. Finally, monitoring studies often conducted after commercialization to validate the safety of a material under actual use conditions. Epidemiological testing is an example, and environmental monitoring using indicator species is another.

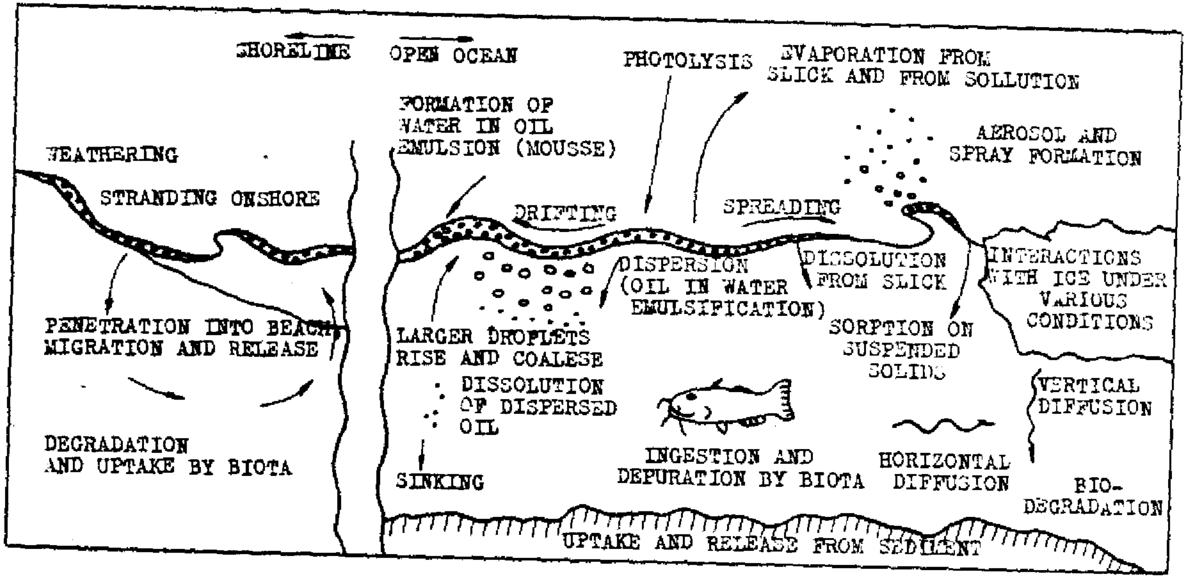
During the screening stage, several chemical parameters must also be measured to obtain an understanding of the transport and fate of the chemical in question. Such information is as important as the toxicity data. While not entirely appropriate, a diagram of the fate of oil spilled at sea demonstrates the complexity of a transport and fate model. Mackay has however attempted to simplify this analysis by developing a fugacity approach, based on the escaping tendency of the chemical.

At the end of the hazard identification stage, some recommendations can be made:

a) The hazard is very high - the toxicity is so high as to warrant discontinuation of developmental testing of the chemical. This recommendation is made when there is no safety margin because the exposure concentration (estimated) exceeds the toxic effect concentration. Very few chemicals fall into this category. In some cases, an altered version of the chemical might be developed and tested. This occurs with drugs and pesticide for-

6300 a

51-2



ENVIRONMENTAL FATE OF OIL SPILLED AT SEA (from Sprogue et al. 1981)

FIG. I

mulations.

b) Hazard is low - no further testing is needed because the margin of safety is judged more than adequate.

c) Hazard is within limits, but - the margin of safety is not as large as would be desired and either additional data are required or management practices must be designed to prevent or reduce exposure.

Obviously the scope of a hazard evaluation should vary depending on the expected use of a compound. An example of the process is found in Figure 3. A chemical of high or intermediate concern would undergo more comprehensive testing. Questions such as these can be asked to define the scope of the problem:

Are there chemicals in the plant that have not been subjected to a hazard evaluation?

Have medical records of employees exposed to these and other chemicals been checked for abnormal trends?

What hazardous chemicals are transported to and from the plant?

Could they be accidentally released resulting in damage to people, the environment and property?

What are the normal discharges of the facility and where do they go?

What wastes are generated at the plant and how are they disposed of?

Are there any potential long or short term hazards to plant employees, the public or the environment during the storage, transport, processing or disposal of these wastes?

What are the company's products that eventually reach the public?

Which of these products could become the subject of liability litigation?

Are there adequate warnings on the labels?

Have all human related accidents been considered in the layout, siting and design of the plant?

With regard to that last question, one very useful technique for evaluating the potential for accidents associated with technology is fault-tree or failure mode and effect analysis. One of the biggest dangers is overlooking a major hazard because one has become too familiar with operations in a plant. A simple example involves the consequences of a pressure relief valve failure as in Fig. 4.

The identification of the sources of a toxic chemical both natural and anthropogenic is obviously very important. Sources should not be discounted until the transport and transformation properties are evaluated in terms of each source and the potential exposure is quantified. There will, of course, be situations in the workplace when a small number of people may be affected but their exposure may be direct and more intensive. Such instances may receive a higher priority ranking for protective or remedial action.

The complexity of the exposure evaluation is highlighted here in the case of mercury. There are at least twelve sources (see Table 1) that one can readily list. The number of people potentially exposed to the different sources, their susceptibilities, and multiple exposures can be estimated. An example of an exposure matrix is given in Table 1.

Figure 3

AN EXAMPLE OF A HAZARD AND EXPOSURE EVALUATION SCHEME

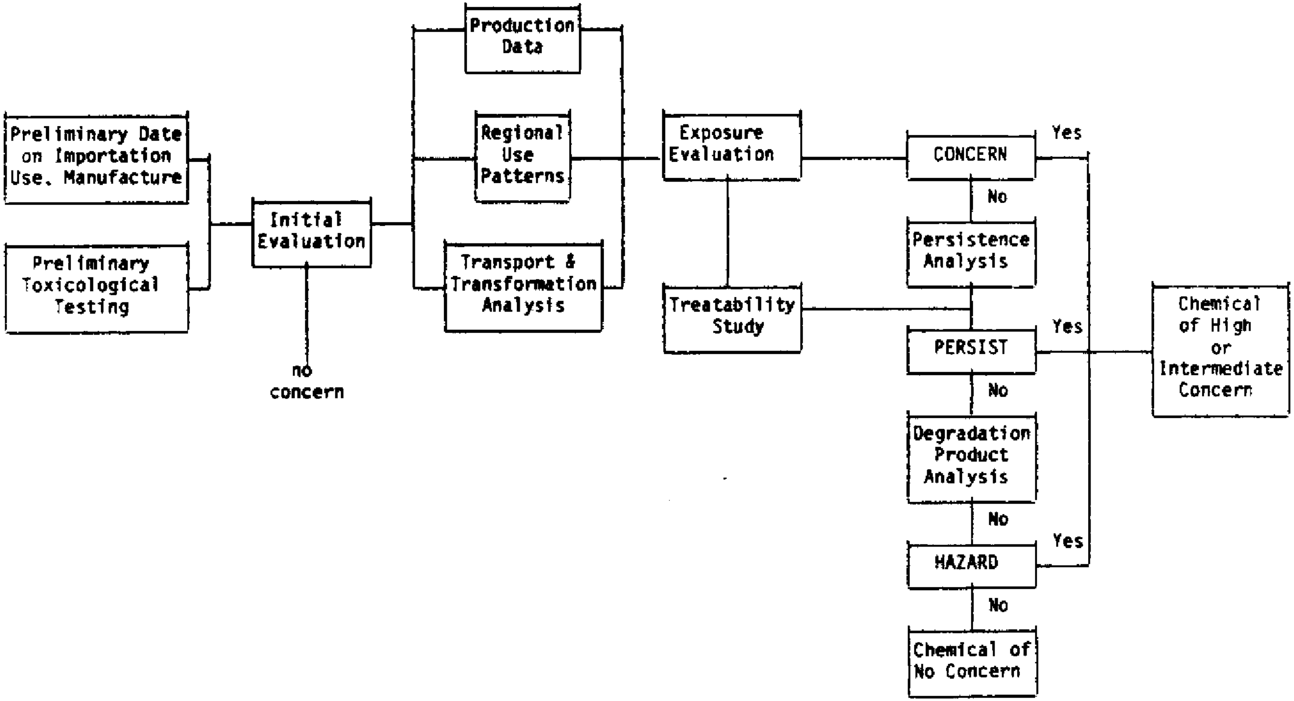


Table 1. SOURCES OF MERCURY

1. Natural geochemical sources
2. Combustion of fossil fuel
3. Fungicides used in agriculture
4. Fungicides used in pulp and paper industry
5. Mercury electrodes in the chlor-alkali industry
6. Electrical equipment such as switches and batteries
7. Uses in medicine and dentistry
8. Refining of mercury from ores
9. Uses in recovering other metals from minerals
10. Antifouling or mildew resistent paints
11. Catalysts in production of acetaldehyde and vinyl chloride
12. Thermometers

RISK QUANTIFICATION

Once the hazards have been identified and exposures estimated, the next step in the decision-making process is to quantify the risk associated with each chemical or event. This is called risk estimation by some authors. Two parameters are important here: the frequencies (usually annual) of an event and the corresponding severity of the accident that one can predict occurring within or outside the plant perimeter. The product of these parameters is a measure of the risk from that hazard.

SEVERITY		FREQUENCY		RISK
(Average Loss per Event)	X	(Expected Number of Events per Year)	=	(Expected Loss per Year)

FAILURE MODE AND EFFECT ANALYSIS

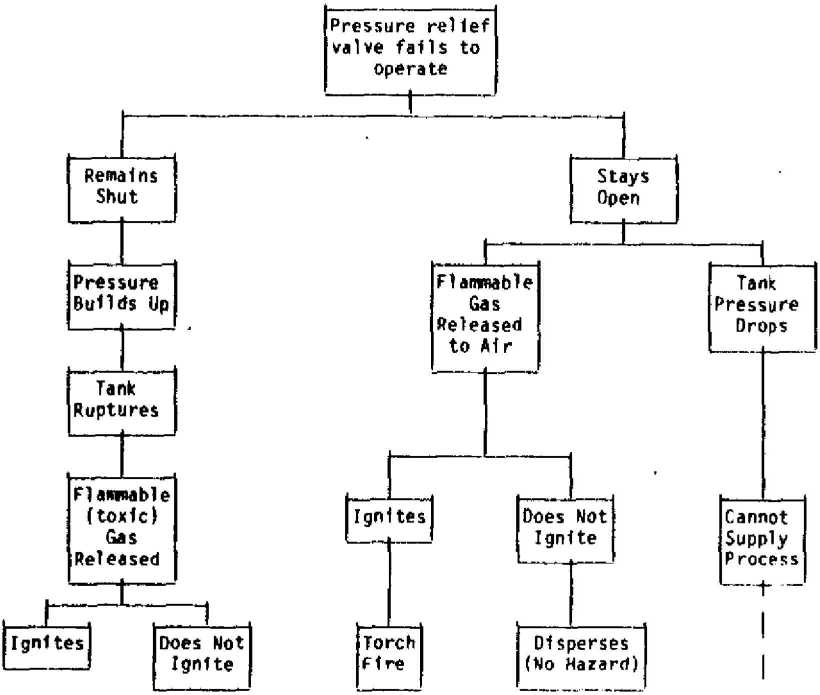


Figure 4

The numbers derived are in probabilities.

Others have calculated risk in the following manner:

HAZARD		PROBABILITY		RISK
(Magnitude of the Health Harm)	X	(Likelihood of the Occurrence)	=	(The average expected total harm for a stated population for a stated period of time)

The major problems in risk qualification today are those accidents associated with toxic chemicals. One aspect is that although the annual frequencies of these occurrences are very small, their consequences or severities may be extremely large. Also there may be a small number of individuals affected at each location but there may be many such plants over the world. The statistics then become the problem. With the exception of a relatively few cases (considering that there are approximately 60,000 chemicals in commercial use today) historical data on such occurrences are too few to be able to predict frequencies or probabilities with any degree of confidence. What we are doing is extrapolating data.

The scope or extent of the risk assessment will depend on a number of items including:

a) Is there a suspected or a known cause or effect?

b) How is the problem distributed geographically (localized, regional, national, international, urban, rural)?

c) How much information is available (fast or slow causes, acute or chronic effects)?

d) Where do effects show themselves (which parts of the environment, which demographic population)?

e) Is the target population normal or particularly susceptible?

f) Are the effects reversible or irreversible based on the limited hazard information available (experiments or extrapolation)?

g) Do the risks arise through a technological process, an environmental process or through human biology and behaviour?

h) Are risks from all sources included when the management of a particular chemical is being considered?

i) What are the smallest effects to be included (death, acute disease, behavioural changes)?

j) What are the longest term effects to be included (immediate damage, one life cycle, several generations)?

You should remember that risk assessments are dynamic, and stated risks may change with new information. The production of toxic chemicals is technology-based and is ever changing. Analytical equipment is more sensitive and accurate than it was ten years ago; safety equipment is more efficient and control technology is more effective.

An over-confidence in current scientific knowledge or those peddling it is one of the limitations of risk assessment. Others are:

- a failure to consider the ways in which human errors can affect technological systems (e.g. Brown's Ferry Nuclear Plant fire in the United States);
- insensitivity of how a technological or ecological system functions as a whole (e.g. recognition of respiratory problems associated with coal fired power plants but not acid rain);

- a failure to anticipate human response to safety measures (e.g. better highways may decrease death toll per vehicle mile but increase total number of deaths because the better highways increase the number of miles driven). (Environment 1979).

At this stage, management alternatives have been identified. A simplistic but effective example is shown in Fig. 6 relating to the use of pesticides for crop protection. There are of course risks associated with each element in the cause-effect chain. As managers, we have to determine the point at which the risks will be reduced to an acceptable level.

THE ACCEPTABILITY OF THE RISK

Recognizing that absolute safety or zero risk is impossible to achieve, one now faces the need to determine which of the chemicals or events presents an acceptable risk to society and the environment and which does not. I should add that this is not the task of the toxicologist; his role is to define the hazard. This is the end point of the analysis that began with the statement that "the hazard is within limits, but...". Because there are several management practices and levels of control (e.g. best practicable technology, as low as reasonably achievable) one has to consider their implications. "Risk cannot be spoken of as acceptable or not in isolation, but only in combination with the costs and benefits that are attendant to that risk!" (Kaplan & Garrick, 1981). Options facing the manager might include the ability to obtain the same benefit in another way with less risk; accepting a larger risk because it brings a substantially reduced cost or increased benefits.

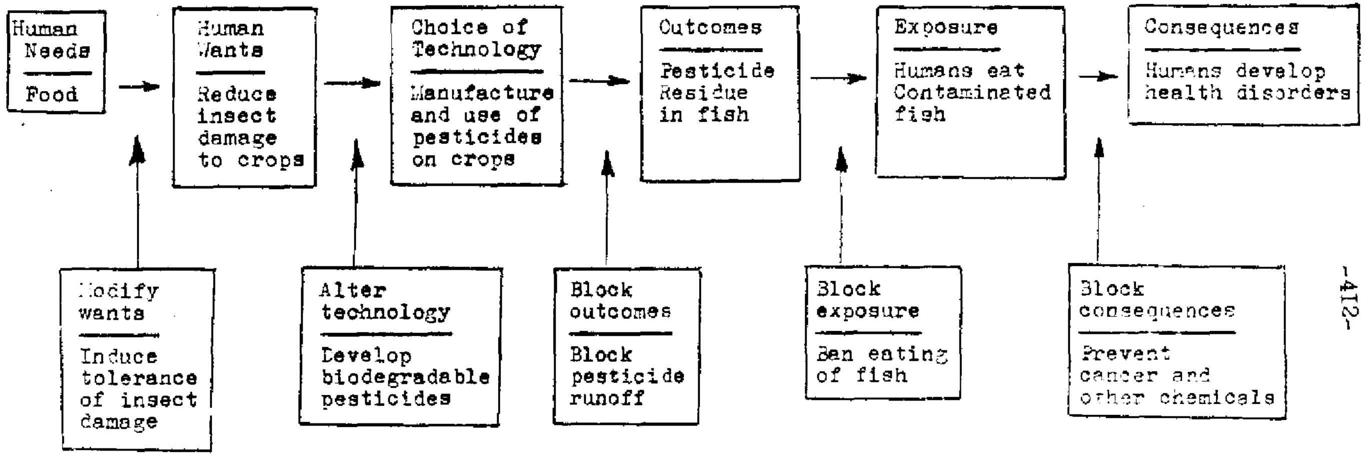


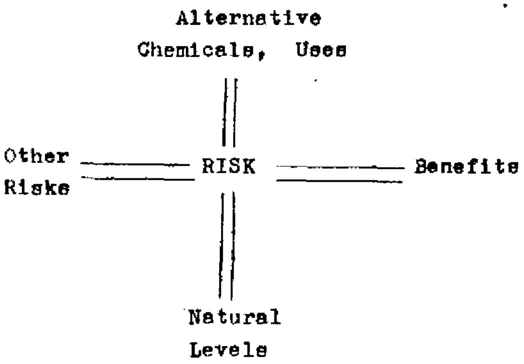
Fig. 6 Model of hazard causation with management options.

It is not unexpected that the risk level that may be acceptable to a corporation is not acceptable to other sectors of society such as the public, the unions, regulatory authorities of insurance companies. That is because these groups perceive risk differently and that is as it should be.

What methods are available for determining the acceptability of the risk?

1. Risk aversion: Maximum reduction of risk possible with little or no consideration of other risks or benefits. This is the case with the concept of zero tolerance and the Delaney clause in the U.S. Food and Drug Act.
2. Risk balancing: Assumes some level of risk above zero is acceptable and defines that level by comparison with appropriate reference cases such as similar technologies, natural background levels or risks previously determined.

Fig. 7 Balancing of risks



Risk can be measured by inquiring into the additional hazard a new chemical, a new formulation, or a new use presents over what already exists or what has been tolerated for long periods of time without apparent ill effects. For example, this is often used to compare radiation from different sources and particularly the natural environment.

Another way to make a risk level meaningful is to describe the alternatives. This works well when the alternatives can be substituted to provide the same good or benefit. As an example, I suggest fiberglass instead of asbestos insulation or red phosphorus instead of yellow phosphorus.

Comparing a risk with other risks by reducing the consequences to a common denominator such as deaths per million persons or death by million passenger miles is another means of balancing risks. This is often used for comparing accident in different types of industries.

Finally one could compare risks with the benefits the chemicals will bring thus greater risks are often accepted where there are greater benefits. The following table illustrates this point (Table 2).

3. Cost effectiveness: This approach seeks to maximize the reduction of risk for each dollar expenditure for safety. Thus if you only have a certain amount of funds, you allocate them to control the various hazards for maximum reduction control. For example, if 100,000 dollars expenditure would save one additional life in one type of accident and 10,000 dollars would be required to save an additional life in a second type of accident, an expenditure of 1,000,000 dollars would be better spent to save 100 lives which could be affected by the second type of accident.

Table 2. FACTORS LEADING TO INCREASED PERCEIVED RISK

i. immediate (observability of damage) rather than latent (e.g. acid rain);

ii. dread (e.g. cancer) versus common (e.g. influenza);

iii. large number of people affect simultaneously (e.g. plane crash) rather than facilities scattered over space and time (e.g. automobile accidents);

iv. a mechanism or process not well understood (e.g. nuclear power);

v. involuntary exposure (e.g. many chemicals in foodstuffs);

vi. children at risk;

vii. threat to future generations (e.g. mutagens and teratogens);

viii. personal threat (e.g. Nimby syndrome);

ix. lack of belief in authority or competence of source of information;

x. benefits not shared by those who bear risks.

Obviously, risk comparisons do not tell the whole story of social acceptability of the risk or the complete spectrum of the social cost. Care need to be taken that estimates of relative health or environmental risk do not conceal value judgements. For example, by lumping together fatalities and injury-days into a single index of health damage.

As I indicated at the beginning of my lecture, managing chemicals or more accurately managing the acceptability of the risks of chemicals, involves other factors than the scientific and technical aspects of toxicology and transport and fate. The task requires a multi-disciplinary approach and in the end, a political decision which has its basis in the philosophy of the government of the day.

The economic aspects have been mentioned in a limited sense and there are different perspectives to consider here both from the micro-economic (the chemical in question and direct effects) and the macro-economic scale involving broader societal issues of commerce, compensation, wages, etc. Legal and legislative remedies must also be considered in any comprehensive management scheme. Can principles of common law such as nuisance and negligence be used to protect the innocent, if the level of risk accepted is greater than is capable of protecting those at high risk, i.e. the sensitive groups in the population? What about current legislation? What about the standards? Can they be monitored effectively?

Last, but not least, the perceptions of the public and of particular elements of the public, must be considered. Several authors (Slovic et al., 1981; Pochin, 1978; Fischoff et al., 1978) have investigated and analyzed the factors involved in public risk perception, factors that must be taken into account in developing a management strategy. Simply put, elected officials put a significant amount of weight on these perceptions. Though the technocrats view them as very subjective, they are in fact legitimate views.

The acceptability of risk can be modified by the ability of industry and government in particular, to reduce that risk. Any management strategy should be developed to optimize that reduction in terms of risk measured in one or more ways, dollar loss per year, deaths per person-year, injury per person-year, etc. Government reaction to a risk problem is also modified by its own philosophies and policies and will often be linked to a concern for the impact of a decision on future regulatory policy.

As stated earlier, one obvious solution to the problem caused by a toxic chemical is the total elimination of the source of the hazard. To achieve this, a corporation must be willing to divest itself of the hazardous product or operation or to recall the hazardous product if it is already on the market. If the chosen approach is to lower the risk to an acceptable level, this could be achieved by altering the chemical and physical properties of the compound or by altering the unsafe practices and procedures in its manufacture, transportation or disposal.

Care must be taken when such solutions are offered, to ensure that the new risk level is indeed lower than the previous risk and that no new hazards are created when the change is made. For example, if a children's nightware material is flammable, additives may be proposed to retard the flammability. That additive could be a skin irritant or cause cancer. If the risk of transporting a toxic liquid waste between two points by tank truck is unacceptable because of traffic congestion and a high population density, the risk might be reduced by using another route, different time schedules or an alternative means of transportation. However, you will have to evaluate the expected frequency of accidents along the new route due to poorer road surfaces, poor lighting at night to ensure that it is slower than in the previous case. Response times may also be a factor.

CONTROL ALTERNATIVES AND STRATEGIES

Whether it be in the workplace, on the farm, in the home, a simple approach can be employed in the design of preventive or remedial measures:

i. identify the characteristics of the problem, i.e. what is happening versus what should happen;

ii. go as far back into the system as possible to solve parts of the problem:
   - process modifications
   - substituting less hazardous chemicals;

iii. after all is done that is feasible, a waste may remain. The cost of handling that waste may necessitate a further review of the materials or process creating that waste:
   - increasing the purity of raw materials (e.g. 2,3,7,8 TCDD in 2,4,5-T);
   - recovery of materials for sale or exchange;

iv. an attempt should be made to reduce and simplify that which must be treated and that which must be disposed of:
   - waste segregation
   - recycle waste water for secondary use
   - recycle process solutions or materials
   - waste concentration;

v. design for that which remains:
   - waste stabilization
   - onsite treatment and disposal
   - offsite treatment and disposal

There are several questions that must be answered in determining what available technology is appropriate to control the chemicals in question. I would identify the following for your consideration:

a. State of development - has the technology been tested extensively in similar conditions?

b. Range of technology applications - can it be used to control various toxic chemicals?

c. Effectiveness - does it control the chemical in question?

d. Process reliability - how much variation in effluent quality and quantity can be treated?

e. Efficiency - does it reduce the chemical by 75%, 90%, 99% on a continuing basis?

f. Environmental acceptability - are you creating a water pollution problem when eliminating an air pollution problem? What kind of residue is created?

From an occupational health and safety perspective, there are a number of protection measures that can be included in the design of new facilities or retrofitted into existing factories. Passive measures include:

1. Layout and siting of the plant to segregate parts of the plant.
2. Automation to separate hazardous concentrations and operations from personnel.
3. Design of tanks, structures and foundations to withstand the worst credible natural events.
4. Use of explosion-proof electrical equipment.
5. Regular preventive maintenance of process equipment and transportation vehicles.
6. Training of employees in standard operating procedures as well as emergency response actions.

7. Regular comprehensive medical examinations.
8. Preparation of contingency plans.
9. Quality control.
10. Corrosion protection of equipment, particularly piping.

Depending on the hazard and potential exposure, several active protection measures can also be included in the design of plants:

1. Detection and alarm systems for release of toxic chemicals, abnormal temperature, pressure excursions.
2. Automatic fire suppression and control equipment.
3. Response to fires, explosions and chemical releases by trained and properly outfitted crews.
4. Automatic shut down of key operations under certain alarm conditions.
5. Utilization of automatic shut off valves when certain abnormal conditions are noted (Atallah, 1980).

COUCLUSION

I have attempted to outline a means of intergrating the information, whether they be facts or assumptions, into a rational process allowing us to make informed decisions about chemicals or operations involving toxic chemicals. That process and on example are described graphically in Fings. 8 and 9. I have also identified several questions that should be asked at the various stages of the procedure. Whenever you have a toxic chemical problem at hand, I would counsel the following:

a. Clearly identify the problem or issue
b. Determine what your objective is
c. List the known facts

d. List the assumptions you can make and the confidence limits for the assumptions
e. Identify alternate solutions
f. Define the environmental and public health significance
g. Define the economic significance
h. Define the social significance (perceptions)
i. Identify the access to the decision-making process
j. Calculate the likelihood of success - if the likelihood is very low, don't waste your time, there are another 59,999 chemicals to worry about.

In concluding, I want to emphasize that if the objective is to manage chemicals and their attendant risks, then you cannot completely separate the industrial from the communal from the agricultural from the ecological environments. Due to their physical and chemical properties, many chemicals move from one category to another, from one medium to another. This reinforces the need for government departments to work together particularly departments of health, environment, agriculture, consumer protection, fisheries, labour and transportation. Obviously, we shouldn't stop there, national governments must cooperate especially in the development of compatible and acceptable data bases such as the IRPTC.

Some would say that toxicologists and toxic chemical managers have an impossible task ahead of them. I'm optimistic, however, that we can put the decision-making processes into place to ensure that we manage the risks effectively.

A famous cartoon character named Pogo once said:
"We have met the enemy and he is us."

Figure 8

THE DECISION MAKING CHAIN IN THE RISK ASSESSMENT PROCESS

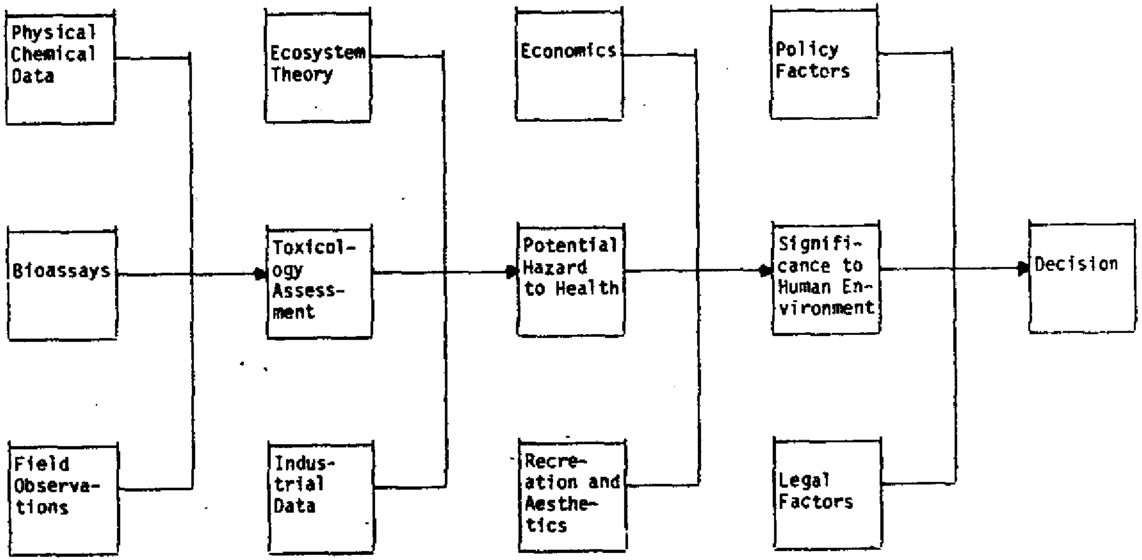
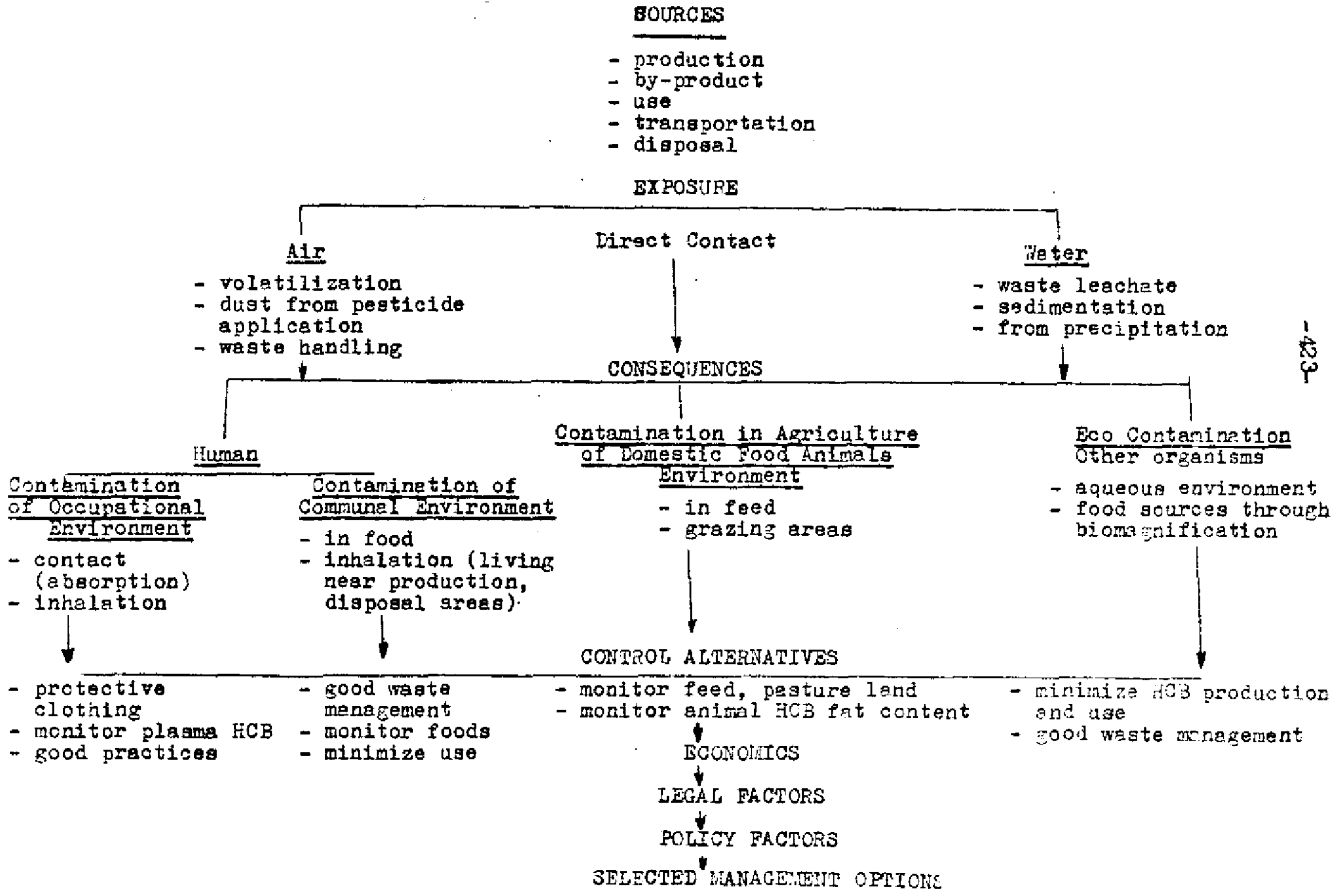
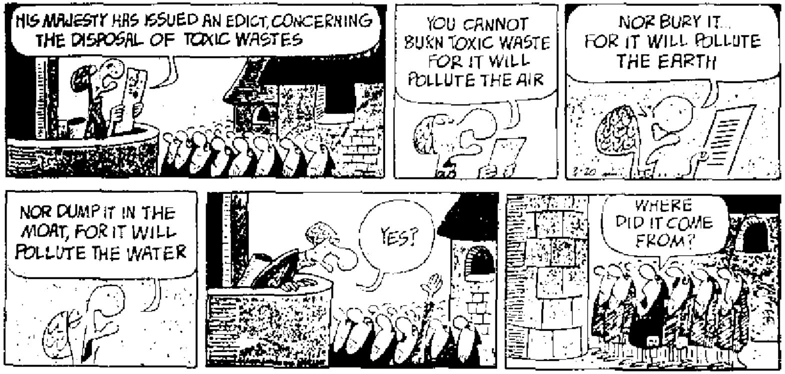


Fig. 9 MANAGEMENT STRATEGY FOR HEXACHLOROBENZENE





The WIZARD of ID

When we can truly say that, in relation to the problems caused by toxic chemicals, we will be on our way to success. Until then, perhaps the Wizard of Id points our the current state-of-the-art (Fig. 8).

REFERENCES

1. Atallah S. Assessing and managing industrial risk. Chemical Engineering, 1980, September, p.94-103.

2. Fischhoff B., Hohenemser C., Kasperson R.E., Kates R.W. Handling Hazards. Environment, 1978, vol.20, N 7, p.16-37.

3. Green H.P. The role of law in determining the acceptability of risk, in R.C.Schuri g, W.A.Albers, Jr. (eds.). Societal risk assessment: How safe is safe enough? Plenum Press, New York, 1980, p.255-269.

4. Harriss R.C., Hohenemser C. Mercury- measuring and managing the risk. Environment, 1978, vol.20, N 9, p.25-36.

5. Hague R.J., Falcon S. Cohen and Riordan C. The role of transport and fate studies in the exposure assessment and screening of toxic chemicals, in R.Hague (ed.). Dynamics, exposure and hazard assessment of toxic chemicals. Ann Arbor Science, Michigan, 1980.

6. Kaplan S., Garrick B.J. On the quantitative definition of risk. Risk Analysis, 1981, vol. , N 1, p.11-27.

7. Kasper R.G. Perceptions of risk and their effects on decision-making in R.C. Schuri g, W.A. Albers, Jr., (eds.). Societal risk assessment: How safe is safe enough? Plenum Press, New York, p.72-84, 1980.

8. Mackey D., Wells P.G. Effectiveness, behaviour and toxicity of dispersants. Spill Control Technology, 1982.

9. Mackay D., Patterson S. Calculating fugacity. Environmental Science and Technology, 1981, vol.15, N 9, p.1006-1014.

10. Munro I.C., Krewski D.R. Risk assessment and regulatory decision-making. Food and Cosmetics Toxicology, 1981.

11. Pochin E.E. The acceptance of risk. Br.Med.Bull., 1975, 31, p.184.

12. Science Council of Canada and Royal Society. 1982. On the appreciation of risk - an overview paper for a symposium on the assessment and perception of health risk in Canada.

13. Slovic P., Fischhoff B., Lichtenstein S. Perceived risk: psychological factors and social implications. Proc.R.Soc. Lond., 1981, A 376, p.17-34.

14. Somers E. The risk from environmental chemicals presented to International symposium on health impacts of different sources of energy. Nashville, Tennessee, IAEA, 1981.

15. Sprague J.B., Vandermeulen J.H., Wells P.G. (eds.). Oil and dispersants in Canadian seas - research appraisal and recommendations. EPS-3-82-2 Environment Canada, 1982, 185 p.

16. Whyte A.V., Burton I. Environmental risk assessment. SCOPE 15, John Wiley, Chichester, 1980.

SOME REGULATORY APPROACHES TO CHEMICAL SAFETY

E. Smith

Chemical Safety can be attained by:

1. Use of toxicologically inert or low toxicity chemicals.
2. Detailed knowledge of the properties of toxic chemicals.
3. Control of really hazardous chemicals.

Chemical Safety is the practical certainty that injury will not result from exposure to a chemical when it is used in the correct manner.

Risk and hazard assessment are based on a range of data.

RISK - The mathematical probability of an event occurring. In toxicology these will be dose-related adverse effects on an individual or a proportion of a population. WHO defines risk as the expected frequency of undesirable effects arising from exposure to a chemical.

Risk may be absolute or relative. Absolute risk is the excess risk due to exposure. Relative risk is the ratio between risk in exposed population and risk in an unexposed population.

HAZARD - The likelihood that a chemical will cause an adverse health effect under the conditions of exposure.

Assessment involves data on:

- Physical Chemical Properties
- Toxicological and Ecotoxicological data
- Type of use(s), extent and quantities
- Mixtures and formulations

Assessment may need to be repeated in the light of new toxicological data, new uses, increased quantities or new formulations.

EUROPEAN COMMUNITY, COUNCIL DIRECTIVE ON DANGEROUS SUBSTANCES

Purpose

The approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous substances (67/548/EEC).

Legal Instrument

"Sixth Amendment" of 1967 Directive, 18th September 1979. Administered by national competent authorities.

Scope

Applies to new substances.

Does not apply to preparations, drugs, cosmetics, food chemicals, pesticides, radioactive material, transport of chemicals or chemicals covered in other Directives.

Objectives

- To protect man and the environment against potential risks, which could arise from the placing on the market of new substances.
- Adequate classification, packaging and labelling of dangerous substances protects the population particularly the workers.

Implementation

- Prescribed data notification; defined quantity thresholds for data requirements.
- A new substance is to be subjected to a prior study by the manufacturer or importer and a notification made to the competent authorities at least 45 days before being placed on the market.
- To apply the Directive an inventory of substances on the market at 18th September 1981 is being compiled. An initial core inventory listing 33,000 chemical substances was circulated in 1982 to be checked against substances, produced or imported, on the European Community market over the period 1971-1981. Any substance not listed on the final inventory will be treated as a new substance for notification purposes. The final inventory will be known as the European Inventory of Existing Commercial Chemical Substances (EINECS).
- Notification in one Member State is valid for the Community. The notification is copied to the European Commission which then copies it to the other Member States.

Classification

- Classification is basically on mammalian LD_{50}/LC_{50} but other significant effects may modify this (e.g. sub-acute or chronic toxicity, carcinogenicity).

Category	Oral LD_{50} rat, mg/kg	Percutaneous LD_{50} rat or rabbit, mg/kg	Inhalation LC_{50} 4 hours, rat, mg/kg
Very toxic	$\leq$ 25	$\leq$ 50	$\leq$ 0.5
Toxic	25 - 200	50 - 400	0.5 - 2.0
Harmful	200 - 2000	400 -2000	2.0 -20.0

Notification Data

Basic Notification

- A Notification (Level 0) must be made when a manufacturer or importer proposes to place on the market 1 tonne of a chemical (Level 0). There are exceptions for polymers with less than 2% monomer and research chemicals for laboratory use or testing purposes.
- There is provision for a Limited Announcement for lesser quantities but related to total quantity on the whole EEC market. This comprises chemical identity, labelling data and quantity. Note that the provision of labelling data requires at least acute toxicity testing. For substances classified as very toxic or toxic, safe handling information and precautions must be provided.

A notifier submits to the national competent authority:

- technical dossier;
- declaration of unfavourable effects;
- proposed classification and labelling;
- recommendation for safe use and precautions.

Further Notification

Additional information and tests may be required where:

a) the quantity placed on the market by a notifier reaches 10 tonnes per year or if there is a total of 50 tonnes (Level 1), and

b) the quantity placed on the market by a notifier reaches 1,000 tonnes per year or a total or 5000 tonnes (Level 2).

The additional tests are specified by the competent authorities.

- Tests are to be conducted on the substance to be marketed according to recognised methods and in compliance with the principles of good laboratory practice. If a test is technically not possible or is not considered necessary the reasons must be stated.

Confidentiality

- The possibilities for keeping data confidential are limited and cannot apply to the physical and chemical data, the interpretation of the toxicological tests nor to the hazards and safety precautions.

Data to be notified in the Level 0 "Base Set"

Technical Dossier

Identity of the Substance

- name;
- empirical and structural formula;
- purity, impurities, additives;
- analytical methods;

Information on use and quantity

- proposed uses;
- functions, effects;
- closed or open system;
- production or imports for each use (tonnes/year)

- recommended procedures for handling, storage, transport, fire precautions, accidental spillage, human poisoning.

Physical Chemical Properties

- melting point;
- boiling point;
- relative density;
- vapour pressure;
- surface tension;
- water solubility;
- fat solubility;
- partition coefficient, n-octanol/water;
- flash point;
- flammability;
- explosive properties;
- auto-flammability;
- oxidising properties.

Toxicological Tests

- acute toxicity (rat) * oral
  * inhalation
  * percutaneous
  * substances other than gases to be administered by the oral route and at least oral route and at least one other route appropriate to human exposure (e.g. volatile liquid might require administration by the oral, percutaneous and inhalation routes);

- skin irritation (rat);
- eye irritation (rabbit);
- skin sensitisation (guinea pig);
- sub-acute toxicity (rat, 28 days);
- mutagenicity and carcinogenicity pre-screen (bacterial and non-bacterial tests);

Ecotoxicological tests

- acute toxicity for fish;
- acute toxicity for Daphnia;
- biotic and abiotic degradation.

Waste Disposal Information

- recovery;
- neutralisation;
- controlled discharge;
- incineration;
- water purification.

Additional Information

The competent authority can require further information and testing to evaluate hazard.

Possible testing for Level 1

Toxicological Tests

- fertility; one species, one or two generations, appropriate route of administration;

- teratology; one species, appropriate route of administration;
- sub-chronic and/or chronic toxicity; one species, appropriate route of administration to examine findings in Level 0 sub-acute test;
- mutagenicity tests, to verify results obtained in Level 0, if positive further testing is required.

Ecotoxicology Tests

- algae, one species;
- prolonged toxicity in Daphnia;
- higher plant;
- earthworm;
- prolonged toxicity in fish, 14 days;
- bioaccumulation, in fish;
- prolonged biodegradation study.

Possible testing for Level 2

Toxicological Tests

- chronic mammalian toxicity;
- carcinogenicity;
- fertility, up to 3 generations if an effect is found in Level 1;
- acute and sub-acute toxicity in a second mammalian species if indicated by findings in Level 1;
- toxicokinetics.

Ecotoxicological Tests

- accumulation, degradation, mobility;
- prolonged toxicity, reproduction, fish;

- acute and sub-acute, birds;
- absorption/desorption for non-biodegradable substances.

USA, TOXIC SUBSTANCES CONTROL ACT

Purpose

To regulate commerce and protect human health and the environment by requiring testing and necessary use restrictions on certain chemical substances and for other purposes.

Legal Instrument

TSCA, 1st January 1977. Administered by the Environmental Protection Agency.

Scope

Applies to old and new chemical substances.

Does not apply to drugs, cosmetics, food chemicals, pesticides , tobacco or radioactive material.

Objectives

- humans and the environment are being exposed to a large number of chemical substances and mixtures and these may be hazardous;
- some chemical substances and mixtures may present an unreasonable risk of injury to human health or the environment in their manufacture, processing, distribution, use or disposal and require control.

Implementation

- The prescribed notification does not automatically include test data.
- For a new substance pre-manufacture or - import notification must be made at least 90 days ahead.
- An inventory of chemicals manufactured in or imported for commercial purposes into the USA in the period 1974-1977 was published in 1979. This numbered 65,000 chemical substances. Any substance not listed is subject to pre-manufacture or import notification. There is a procedure for revising and updating the inventory.

Important Sections

Section 4 - Testing of Chemical Substances
Section 5 - Pre-manufacture Notification
Section 6 - Regulation of Hazardous Chemicals
Section 8a - General Reporting
Section 8b - Chemical Inventory
Section 8c - Records of Adverse Reactions
Section 8d - Health and Safety Studies
Section 8e - Substantial Risk Reporting

Section 4

To require test data the Administrator of EPA must find either:

(i) that the manufacture, distribution, use or disposal of a chemical substance or mixture may present an unreasonable risk of injury to human health or the environment, or

(ii) that there are <u>insufficient data</u> or experience to determine or predict hazard.

If testing is required it must include the chemical identity and must follow standard test procedures. There are standard procedures for toxicological tests.

<u>Unreasonable risk</u> is not defined but represents a judgement based on the probability, severity and extent of possible harm to the human population and the environment taking into account the possible benefits to society.

If the data are already available the notifier may share the expense with the first and other notifiers and need not do actual testing.

Notified test data are published including chemical identity, uses and other test results.

A Priority List of chemical substances or mixtures requiring testing can be compiled by the Administrator.

Where the Administrator receives data or other information that there is a significant risk of serious or widespread harm to humans from cancer, gene mutations or birth defects action must be taken within <u>180-270 days</u>.

<u>Section 5</u>

- A premanufacture notification (PMN) must be submitted to EPA at least 90 days before manufacture or input. A PMN is also required for a <u>significant new use</u> of an existing chemical substance.

- A PMN must contain reasonably ascertainable information about chemical identity, physical chemical properties, manufacturing process, annual production volume, uses, health and environmental effects.
- EPA must review the PMN, make a risk assessment and inform the notifier within 90 days if there is evidence of unreasonable risk to health or the environment.

Section 6

- EPA can regulate manufacture, processing, distribution, use or disposal of any chemical substance or mixture which presents an unreasonable risk to health or the environment.
- Regulatory control measures include banning, limited manufacture, reduced worker exposure, limited uses, hazard labelling and restricted disposal.

Section 8

8a. Manufacturers or processors of chemical must maintain records and submit reports.

8b. Manufacturers or importers must report the identity and site of manufacture of chemicals. An inventory was published in 1979 and is updated as new chemicals come through the PMN procedure.

8c. Companies must keep records of significant adverse reactions from exposure to a chemical.

8d. Chemical manufacturers, processors, distributors and others can be required to submit health and safety data to EPA for assessment purposes (e.g. industrial hygiene studies, measurements of exposure to a chemical).

8c. Any information supporting a conclusion that a chemical substance or mixture presents a substantial risk of injury to health or the environment must be reported (e.g. new evidence of carcinogenicity or birth effects).

Confidentiality

In general the notified information is freely available. Notifiers may request that "trade secrets" (e.g. method of production, composition) are kept confidential but the Administrator of EPA may disclose such information if it is necessary to protect health or the environment against an unreasonable risk. Health and Safety information cannot be kept confidential.

ORGANISATION FOR ECONOMIC COOPERATION AND DEVELOPMENT (OECD)

Chemical Safety Aspects

OECD is an advisory not a regulatory body.

Development of a Chemical Safety Programme

1974	Recommendation on the assessment of the potential environmental effects of chemicals. Prior to the marketing of chemicals and chemical products the potential effects on humans and the environment should be assessed.
1977	Recommendation establishing guidelines in respect of procedure and requirements for anticipating the effects of chemicals on man and the environment.

- Harmonised approach to testing.

1978 Decision on a Special Programme on the control of chemicals.

- Agreed test methods.
- Agreed Good Laboratory Practice.
- Inter acceptability of data.
- Agreed approach to interpretation.

1981 OECD Guideline methods for testing chemicals.

1982 Decision on the minimum pre-marketing set of data for the assessment of chemicals.

- An agreed set of tests for the use or guidance (flexible application) of member countries.

Objectives

- To protect man and the environment from exposure to hazardous chemicals.
- To ensure the most effective testing of chemicals taking into account the available facilities and specialist manpower resources.
- To avoid unnecessary duplication of testing.

Minimum Pre-Marketing Set of Data (MPD)

Intended as a first step in a sequenced or tiered testing system. In theory this is the most effective approach because only necessary testing is performed. In practice the difficulty of obtaining agreement on the decision or trigger points involved in moving from one test or one tier to another has slowed progress.

1. The first tier comprises screening tests and looks for effects.

2. Subsequent tiers comprise tests to confirm or extend the results of previous tests.
3. MPD provides data for a meaningful first assessment of the potential hazard of a chemical to health and the environment before a decision is taken to place it on the market.

Hazard Assessment for Chemicals

OECD defines the hazard of a chemical as a function of two broad considerations:

i) the potential of a chemical to harm biological systems (or damage other systems), and

ii) its potential for exposure such that harm or damage can occur.

Isolated partial hazard assessments could be made on the data from individual tests but it is better to make a broader assessment on data from a number of tests.

Data Components for OECD MPD

- Chemical identification

  Name
  Structural formula
  CAS - number
  Spectra (pure and technical grade)
  Purity (technical grade)
  Impurities (% age by weight)
  Additives and Stabilisers (% age by weight)

- Production / Use / Disposal Data

  Estimated production, tonnes/year

Intended uses

Suggested disposal methods

Expected mode of transport

- <u>Recommended precautions and emergency measures</u>

- <u>Analytical methods</u>

- <u>Physical /Chemical data</u>

Melting point

Boiling point

Density

Vapour pressure

Water solubility

Partition coefficient

Spectra

Dissociation constant

Screening for:

* Hydrolysis

* Adsorption/Desorption

* Particle size

- <u>Toxicity Data</u>

1) Acute toxicity:

oral

dermal

inhalation

Skin irritation

Skin sensitisation

Eye irritation

ii) Repeated dose, 14-28 days:

Appropriate route

iii) Mutagenicity:

Minimum of two tests for gene and chromosome effects

- **Ecotoxicity data**

Fish LC_{50} (at least 96 hours exposure)
Daphnia reproduction (14 days)
Algae growth inhibition (4 days)

- **Degradation / Accumulation data**

Biodegradation (screening phase)
Bioaccumulation (screening phase data:
n-octanol/water partition
fat solubility
water solubility
biodegradability)

Updating Procedure

- to take account of new developments in science and experience of chemical notification schemes;
- to modify test methods or introduce new methods.

Existing Chemicals Programme

- To exchange information
- To identify chemicals which present hazards to man and the environment
- To identify testing needs.

PIK VINITI No. 6300a