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Grigory M. Franchuk, D.E., Prof.
Margaryta M. Radomska, post-graduade student

EXPOSURE MODELLING IN RISK ASSESSMENT OF INDUSTRIAL ENTERPRISES

The provisions and theory of exposure assessment are presented in the article. According to basic directions of exposure assessment methods and necessary data are defined. The elements of exposure modeling for different environments and systems of human body are developed. Practical application of exposure and dose definition to the process of environmental risks assessment process is given.

Розглянуто основні положення і теорія оцінки враження. Визначено основні підходи і необхідні дані для виконання різних типів оцінки враження. Розроблено компоненти моделювання враження, пов'язаного з основними компонентами навколишнього середовища і системами людського організму. Наведено результати розрахунку доз і враження в процесі оцінки ризиків.

dose, exposure, modelling, risk assessment

Introduction

There are a number of different purposes for exposure assessments, including their use in risk assessments, toxicology, trends analysis and epidemiology. Official guidelines and regulations in this field are intended to convey the general principles of exposure assessment, not to serve as detailed instructions. As a result, it is necessary to adjust general rules to the specific characteristics of industries and industrial objects as they can be considered the main sources of pollutants threatening to human health.

Background information analysis

Exposure assessment in various forms dates back to the early XXth century in the fields of epidemiology, industrial hygiene, and health physics [1−3]. Epidemiology is the study of disease occurrence and the causes of disease, while the latter fields deal primarily with occupational exposure. Exposure assessment combines elements of all three disciplines. This has become increasingly important since the early 1970s due to greater public, academic, industrial, and governmental awareness of chemical pollution problems. Corresponding regulations and directives were developed by those national and global organizations, which deal with environmental issues in relation to human health hazards [4−5]. Application of this standards shows the need to amend them from time to time in order to keep them in accordance with the newest scientific achievements.

As for Ukraine and neighbouring countries, we do not have similar standards accepted and implemented at all levels of the state environmental safety provision. The necessary regulations must be developed to standardize the process of risk assessment, which is based on exposure assessment.

Problem formulation

Mostly exposure assessment is used in toxicological investigations to define possible consequences of poisoning, but this way the investigation is not connected with initial sources of poison. The process of assessment of environmental risks imposed by technogenic sources usually ends up with calculation of negative results probabilities and their magnitude. Exposure assessment may give information about these negative results in more detailed form by calculating both doses and reactions related to certain chemicals and the exposure routes attributed to certain types of industrial enterprises or pollution sources in general.

Concept and methods

The human exposure means contact of the chemical or agent with the visible exterior of the person (skin and openings into the body such as mouth and nostrils), or the so-called exchange boundaries where absorption takes place (skin, lung, gastrointestinal tract) [6]. The EEA and the EPA prefer to define exposure as in the approach [4].

As a result, exposure assessment is the quantitative or qualitative evaluation of that contact. It describes the intensity, frequency, and duration of contact, and often evaluates the rates at which the chemical crosses the boundary (chemical intake or uptake rates), the route by which it crosses the boundary (exposure route; dermal, oral, or respiratory), and the resulting amount of the chemical that actually crosses the boundary (a dose) and the amount absorbed (internal dose).

Depending on the purpose, for which an exposure assessment will be used, the numerical output of the exposure assessment may be an estimate of either exposure or dose. If exposure assessments are done as part of a risk assessment that uses a dose-response relationship, the output usually includes an estimate of dose.

Other risk assessments, for example many of those done as part of epidemiologic studies, use empirically derived exposure-response relationships, and may characterize risk without the intermediate step of estimating dose. Table provides the summary of the exposure and dose terms along with examples of units commonly used in environmental investigations.

Although exposure assessments are done for a variety of reasons, the quantitative exposure estimation can be approached from three different ways:

− the exposure can be measured at the point of contact (the outer boundary of the body) while it is taking place, measuring both exposure concentration and time of contact and integrating them (point-of-contact measurement);

− the exposure can be estimated by separate evaluation of the exposure concentration and the time of contact, then combining this information (scenario evaluation);

− the exposure can be estimated from dose, which in turn can be reconstructed through internal indicators (biomarkers, body burden, excretion levels, etc.) after the exposure has taken place (reconstruction).

These three ways are approaches for arriving at a quantitative estimate of exposure. Sometimes the approaches to assessing exposure are described in terms of "direct measures" and "indirect measures" of exposure. Measurements that actually involve sampling on or within a person, for example, use of personal monitors and biomarkers, are termed "direct measures" of exposure. Use of models, environmental measurements, and questionnaires, where measurements do not actually involve personal measurements, are termed "indirect measures" of exposure. The direct/indirect nomenclature focuses on the type of measurements being made: the scenario evaluation/point – of – contact / reconstruction nomenclature focuses on how the data are used to develop the dose estimate.

These three approaches to quantification of exposure (or dose) are independent, as each is based on different data. The independence of the three methods is a useful concept in verifying or validating results. Each of the three has strengths and weaknesses; using them in combination can considerably strengthen the credibility of an exposure or risk assessment.

Exposure modelling

Here we focused on exposure via inhalation, oral intake, and dermal absorption as these routes are related to environmental factors.

The process of a chemical entering the body can be described in two steps: contact (exposure), followed by actual entry (crossing the boundary). Absorption, either upon crossing the boundary or subsequently, leads to the availability of some amount of the chemical to biologically significant sites within the body (internal dose).

Although the description of contact with the outer boundary is simple conceptually, the description of a chemical crossing this boundary is more complex.

There are two major processes by which a chemical can cross the boundary from outside to inside the body. Intake involves physical moving the chemical through an opening in the outer boundary (usually the mouth or nose), typically via inhalation, eating, or drinking. The chemical intake rate is the amount of chemical crossing the outer boundary per unit time, and is the product of the exposure concentration times the ingestion or inhalation rate.

The second process by which a chemical can cross the boundary from outside to inside the body is uptake. Uptake involves absorption of the chemical through the skin or other exposed tissue such as eyes. Although the chemical is often contained in a carrier medium, the medium itself typically is not absorbed at the same rate as the chemical. Uptake through the lung, gastrointestinal tract, or other internal barriers also can occur following intake through ingestion or inhalation

The conceptual process of contact, then entry and absorption, can be used to derive the equations for exposure and dose for all routes of exposure.

In general exposure over some period can be represented by a time-dependent profile of the exposure concentration [7]:

$$\mathrm{E} = \int_{t_1}^{t_2} C(t)dt ,$$

where

E is the magnitude of exposure;

$C(t)$ is the exposure concentration as a function of time;

$t_2 - t_1$ the exposure duration ED.

If ED is a continuous period of time (e.g., a day, week, year, etc.), then $C(t)$ may be zero during part of this time. Contact time is the actual time periods (events, episodes) during which actual exposure is taking place. Integrated exposures are done typically for a single individual, a specific chemical, and a particular pathway or exposure route over a given time period. An exposure pathway is the course a chemical takes from its source to the person being contacted.

The general equation for potential dose for intake processes, e.g., inhalation and ingestion is the integration of the chemical intake rate over time:

$$D_{pot} = \int_{t_1}^{t_2} C(t)IR(t)dt , \quad (1)$$

where

D_{pot} is potential dose;

$IR(t)$ is the ingestion or inhalation rate.

Summary of exposure and dose terms

Term	Refers to	Generic units	Specific example units
Exposure	Contact of chemical with outer boundary of a person, e.g., skin, nose, mouth	Concentration x time	Dermal: (mg/L water) · (hrs of contact), (mg /kg soil) · (hrs of contact). Respiratory: (ppm in air) · (hrs of contact), (μg/m3 air) · (days of contact). Oral: (mg /L water) · (min of contact), (mg /kg food) · (min of contact).
Potential dose	Amount of a chemical contained in material ingested, air breathed, or bulk material applied to the skin	Mass of the chemical: Dose rate is mass of the chemical/time; mass of chemical/unit body weight · time	Dermal: (mg /kg soil) · (kg soil on skin) = mg in soil applied to skin. Respiratory: (μg/m3 air) · (m3 air breathed/min) · (min exposed) = μg in air breathed. Oral: (mg/L water) · (L water consumed/day) · days exposed = mg ingested in water (also dose rate: mg/day)
Applied dose	Amount of chemical in contact with the primary absorption boundaries (e.g., skin, lungs, gastrointestinal tract) and available for absorption	As above	Dermal: (mg/kg soil) · (kg soil directly touching skin) · (%of chemical in soil actually touching skin) = mg actually touching skin. Respiratory: (mg/m3 air) · (m3 air directly touching lung) · (%of chemical actually touching lung) = mg actually touching lung absorption barrier. Oral: (mg/kg food) · (kg food consumed/day) · (% of chemical touching g.i. tract) = mg actually touching, g.i. tract absorption barrier (also absorbed dose rate: mg/day), chemical available to organ or cell (dose rate: mg available to organ/day)
Internal (absorbed) dose	The amount of a chemical penetrating across an absorption barrier or exchange boundary via either physical or biological processes	As above	Dermal: mg absorbed through skin, mg absorbed via lung. Respiratory: mg absorbed via g.i. tract
Delivered dose	Amount of chemical available for interaction with any particular organ or cell	As above	Oral: dose rate: mg absorbed/day or mg/kg · day Mg available to organ or cell (dose rate: mg available to organ/day)

Equation (1) can also be expressed in discrete form as a summation of the doses received during various events *i*:

$$D_{pot} = \sum_i C_i \cdot IR_i \cdot ED_i , \quad (2)$$

where
ED_i is the exposure duration for event *i*.
If *C* and *IR* are nearly constant (which is a good approximation if the contact time is very short), equation (2) becomes:

$$D_{pot} = \overline{C} \cdot \overline{IR} \cdot ED , \quad (3)$$

where
ED is the sum of the exposure durations for all events, and $\overline{C}$ and $\overline{IR}$ are the average values for these parameters.
Equation (3) is used in cases where *C* and *IR* vary considerably and (2) can be used if the exposure can be broken out into segments, where *C* and *IR* are approximately constant. If even this condition cannot be met, equation (1) may be used.
Doses may be expressed in several different ways. For risk assessment purposes, estimates of dose should be expressed in a manner that can be compared with available dose-response data.
Solving equations (1)–(3), for example, gives a total dose accumulated over the time in question.
Exposure assessments should take into account the time scale related to the biological response. For many noncancer effects, risk assessments consider the period of time, over which the exposure occurred, and often, if there are no excursions in exposure that would lead to acute effects, average exposures or doses over the period of exposure are sufficient for the assessment. These averages are often in the form of average daily doses (ADDs).
An ADD can be calculated from equation (1) by averaging Dpot over body weight and averaging time, provided the dosing pattern is known so the integral can be solved, which happens not very often. Using equation (3) instead of (1) or (2) involves making steady-state assumptions about *C* and *IR*, but this makes the equation for ADD easier to solve. For intake processes equation (3) becomes:

$$ADD_{pot} = [\overline{C} \cdot \overline{IR} \cdot ED] / [BW \cdot AT] , \quad (4)$$

where
ADD_{pot} is the average daily potential dose;
BW is body weight;
AT is the time period over which the dose is averaged (converted to days).

For effects such as cancer, where the biological response is usually described in terms of lifetime probabilities, even though exposure does not occur over the entire lifetime, doses are often presented as lifetime average daily doses (LADDs). The LADD takes the form of equation (4), with lifetime (LT) replacing the averaging time (AT). The LADD is a very common term used in carcinogen risk assessment where linear nonthreshold models are employed.
For absorption processes, two methods can be used for calculating internal dose. The first, commonly used for dermal absorption from a liquid where at least partial immersion occurs, is derived from the equation for internal dose, D_{int}:

$$D_{int} = \int_{t_1}^{t_2} C(t) \cdot K_p \cdot SA(t) dt ,$$

where
Kp is the permeability coefficient;
SA is the surface area exposed.
Both *C* and *SA* vary over time, and *Kp* vary not over time, but over different parts of the body. Permeability coefficient expresses relationship between the flow and the exposure concentration and is experimentally measurable. The flow means the flux of the chemical across the barrier, it is not directly measurable, and dependents on nature of chemical and barrier, active transport versus passive diffusion processes, and concentration of the chemical contacting the barrier. Thus the internal dose is:

$$D_{int} = \overline{C} \cdot K_p \cdot \overline{SA} \cdot ED ,$$

where
$\overline{SA}$ is average surface area exposed;
ADD_{int} (average daily internal dose defined from the relation of D_{int} with body weight and time period as in (3)).
The second method of calculating internal dose uses empirical observations or estimation of the absorption rate. It is useful when a small or known amount of material (such as a particulate) or a chemical (such as a pesticide) contacts the skin. The potential dose of a chemical to the skin, D_{pot}, can often be calculated from knowing the concentration, *C*, and the amount of carrier medium applied, M_{med}, either as a whole or on a unit surface area basis.

Thus, potential dose from dermal contact with soil can be calculated using the following equation:

$$D_{pot} = \overline{C} \cdot M_{med} = \overline{C} \cdot F_{adh} \cdot \overline{SA} \cdot ED ,$$

where

M_{med} is amount of soil applied;

F_{adh} is the adherence factor for soil (the amount of soil applied to and adhering to the skin on a unit surface area per unit time).

The relationship between potential dose and applied dose for dermal exposures is that potential dose includes the amount of the chemical in the total amount of medium contacting the skin, and applied dose includes only that amount of the chemical, which actually directly touches the skin:

$$D_{pot} = D_{app} \int_{t_1}^{t_2} f(t)dt , \quad (5)$$

where

$f(t)$ is nonlinear absorption function, usually not measurable, having the dimensions of mass absorbed per mass applied per unit time.

The absorption function will vary due to a number of factors (concentration gradient of chemical, carrier medium, type of skin, skin moisture, skin condition, etc.). If $f(t)$ could be integrated over time from the start of exposure until time T, it would yield the absorption fraction, AF, which is the fraction of the applied dose that is absorbed after time T. The absorption fraction is a cumulative number and can increase with time to a possible maximum of 1 (or 100% absorption), but due to competing processes may reach steady state long before reaching 100 % absorption.

Equation (5) then becomes

$$D_{int} = D_{app} \cdot AF$$

and if all the chemical contained in the bulk material are assumed to come in contact with the skin eventually, then D_{app} equals D_{pot} and

$$ADD_{int} = [\overline{C} \cdot M_{med} \cdot AF\ ] /[\ BW \cdot AT\ ]$$

or

$$D_{int} = D_{pot} \cdot AF .$$

This approximation will by no means always give credible results: unfortunately, almost no data are available concerning the relationship between potential dose and applied dose for dermal exposures. Experimental data on absorption fractions derived for soil commonly use potential dose rather than applied dose, which may make the experimental data at least in part dependent on experimental conditions such as how much soil was applied.

In general, not all data necessary for calculation performance are known and available (especially, if we consider subsequent transformations and transfer processes within the organism, for example, chemicals in air, food, or drinking water normally enter the body through the intake processes, and then are absorbed through internal uptake in the lung or gastrointestinal tract). So, common assumption is that for intake processes, the potential dose equals the applied dose. Although arguments can be made that this assumption is likely to be more nearly accurate than for the case of soil contact, the validity of this assumption is unknown at this point. Essentially, the assumption of equality means that whatever is eaten, drunk, or inhaled touches an absorption barrier inside the person. As a result the following equations can be formed:

$$D_{int} = D_{app} \cdot AF = D_{pot} \cdot AF = \overline{C} \cdot \overline{IR} \cdot ED \cdot AF ;$$

$$ADD_{int} = [\ \overline{C} \cdot \overline{IR} \cdot ED \cdot AF\ ] /[\ BW \cdot AT\ ] .$$

Although equations for calculating exposure, dose, and their various averages are in widespread use in exposure assessment, the assessor should consider the implications of the assumptions used to derive the equations. Simplifying assumptions used in deriving the equations may mean that variations in exposure concentration, ingestion or inhalation rate, permeability coefficient, surface area exposed, and absorption fraction can introduce error into the estimate of dose if average values are used, and this must be considered in the evaluation of uncertainty.

Depending on the use of the exposure assessment, estimates of exposure and dose in various forms may be required. In case of industrial enterprise there are three acceptable directions of modelling and calculations.

1. Exposure concentrations are useful when comparing peak exposures to levels of concern such as short-term exposure limits, permissible levels of influence and so on.

2. Exposure or dose profiles describe the exposure concentration or dose as a function of time. Concentration and time are used to depict exposure, while amount and time characterize dose; graphical or tabular presentations may be used for either type of profile. Such profiles are very important for use in risk assessment where the severity of effect is dependent on the pattern by which the exposure occurs rather than the total (integrated) exposure.

For example, a developmental toxin may only produce effects if exposure occurs during a particular stage of development. Similarly, a single acute exposure to very high contaminant levels may induce adverse effects even if the average exposure is much lower than apparent no-effect levels.
Integrated exposures are useful when a total exposure for a particular route is needed. The integrated exposure is the total area under the curve of the exposure profile. Exposure profile (a picture of exposure concentration over time) contains more information than an integrated exposure (a number), including duration and periodicity of exposure, peak exposure, and shape of the area under the time-concentration curve.

Conclusion

Exposure and dose information are often combined with exposure-response or dose-response relationships to estimate risk, the probability of an adverse effect occurring for different technogenic objects. There is a variety of risk models, with various mathematical relationships between risk and dose or exposure. A major function of the exposure modelling as part of risk assessment is to provide the exposure or dose values, and their interpretations.
The offered modelling provisions give possibility to evaluate human health hazard coming from certain type of industrial enterprises via the most important environmental components, which are water, air and soil, to the dominant exposure path-ways – inhalation, indigestion and dermal contact.
The exposure and dose information available allow estimates of individual risk or population risk, or both. Risk assessments almost always deal with more than a single individual. Frequently, individual risks are calculated for some or all of the persons in the population being studied, and are then put into the context, where they fall in the distribution of risks for the entire population.
As a result, the assessor is able to answer such questions: are there individuals at risk from exposure to the substances under study; to what risk levels are the persons subjected; and what is the average individual risk? In addressing these questions, risk descriptors may give estimation of the probability that an individual in the high end of the distribution may suffer an adverse effect; probability that an individual at the average risk may suffer an adverse effect; or probability that an individual will suffer an adverse effect given a specific set of exposure circumstances. All these calculations and modelling results are of the greatest interest to risk managers when considering various actions to mitigate risk.

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