2

Epidemiological tools

Introduction

Epidemiologists investigating the consequences of chemical incidents must consider the following activities:

- identifying the target population (the population affected by the incident)
- characterizing the exposure (qualitatively and quantitatively)
- defining the health impacts (qualitative and quantitative, acute and chronic).

This chapter discusses each of these in the context of the response to an incident. Epidemiological studies of chemical incidents are subject to special constraints such as time, availability of resources, public anxiety and political influences. The constraints differentiate epidemiological studies following the incident, and the methods used from those applied in less acute situations.

Population at Risk

Definition

The epidemiologist is concerned with a broader population group than that comprising the people obviously affected by an incident. This is the population at risk, the people who might have been exposed to the chemicals by being present in the affected area at the time of the incident. Personal characteristics may determine the extent of exposure or susceptibility to health effects. These may restrict the population at risk to a section of all the people exposed (for example, to women of reproductive age in case of a release of a teratogenic agent). In practice, however, such specific information about an incident is rarely available

when it occurs. Determination of the population at risk will thus be influenced by:

- information about the nature of the incident (the media affected and the toxic properties of the chemical(s) involved);
- the estimate of spatial distribution of the contamination, depending on the dispersion of the pollutant in the environment; and
- the available demographic information (census data, address registry, etc.) and the method of identifying places of residence in the existing data sources (district identification, postal zone identifier, etc.).

The population at risk must be identified for three purposes. The first is to define the population in which the health effects due to the incident may be expected. These people may need special medical care. One can assume that the people obviously affected by an incident can be easily identified by the rescue teams, family members, neighbours or co-workers, and will be provided with medical assistance. Other affected people may show less specific symptoms and, without information about the potential exposure, may not receive optimal medical care.

Second, the population at risk must be identified to determine the target population for studies assessing the effects of the incident. The primary objective is to determine the number of people at risk in order to define the denominator for the calculation of the frequency of the symptoms that may be due to the exposure. The rates can be compared with those in the reference populations: those not affected by the incident.

The third purpose is to define the essential characteristics of the study design to be applied, and to estimate the resources, means and networks required to investigate the health impact.

Precisely defining the population at risk is not an easy task. Including too many unexposed people may diffuse the efforts of medical services and will decrease the impact estimates. If the population selected includes only some of those exposed (only those with higher doses, for example), the severity of the impact may be overestimated. If the effects are specific for a part of the population (such as people in certain occupations), the study should concentrate on that group. The specific hazard may be

difficult to identify early in the investigation, however, and the restriction of the study to a predefined subset of those exposed may reduce its ability to reflect the real magnitude of the health effects.

Since the interpretation of the evaluation will depend on the composition of the study groups, the definition of the population should be clearly stated and recorded for future reference.

The most frequently used methods of determining the size of the population at risk are based on indirect methods of exposure assessment readily available soon after the incident. A useful tool is dispersion modelling, combined with data on the population density in the area of the incident. Models and the population database should ideally be prepared in advance, preferably assisted by a computer-based geographical information system (GIS) facilitating the making of estimates.

Consideration should be given to the inclusion of subjects exposed in special circumstances, such as members of the rescue teams.

Rapid appraisal

When the rescue team has little information about the size of the possibly affected population, the nature or severity of the incident, or the chemicals involved and their toxic properties, the rapid appraisal method may be helpful. This was the case after the Bhopal accident, when a team of doctors travelled in the possibly affected area meeting many people and asking each person a few basic questions *(8)*.

In rapid appraisal, the population surveyed may not be determined beforehand and can be modified according to the information collected. Appraisal can be based on reports from affected people who make telephone enquiries for advice (to general practitioners, casualty departments, emergency services, etc.), as well as those going to physicians' offices or casualty units for assessment. Coordination of the various sources of information on health effects would be helpful in these cases, and gives an early picture of the type and extent of problems occurring, which indicates the extent of the population at risk. Such appraisals may also be needed in a population apparently not affected by the incident, to establish reference health characteristics for the exposed group.

Rapid appraisal may be of value in the early stage of the assessment, but may be biased by the non-representative selection of the contacted persons and gives no quantitative estimate of the magnitude of the health impact of the incident. To establish the distribution and symptoms attributable to the exposure, assessment must be conducted in a pre-defined population at risk; this may exceed the framework of the rapid appraisal.

Sources of demographic information

Assuming that at least approximate information on the area affected by the chemicals released in an incident is available, the size of the population at risk must be estimated from demographic databases. For each population, there may be several sources of demographic information. The source used will depend on accessibility and the importance of its advantages and disadvantages in a given population. In each event, the possibility should be considered that non-registered people, such as commuting workers or travellers, constitute a significant part of those exposed and may influence the actual size of the population at risk.

Access to demographic data in the planning and preparedness phase

Estimating the size of the population at risk immediately after an incident requires rapid access to demographic data. This will depend on the familiarity of the emergency response team, and of the epidemiologist in particular, with the existing data sources. Thus, important tasks of the epidemiologist at the preparedness phase include:

1. identifying all relevant sources of demographic information at the smallest possible geographical scale;
2. assessing the purpose, scope and limitations of each of the available data sources;
3. exploring methods of gaining access to the information (restrictions, speed, necessary equipment, personnel);
4. identifying the format of the data provided by each of the sources;
5. defining situations in which a particular data source should be approached; and
6. specifying the information (contents, format, level of details) to be collected from each source in the case of an incident.

The purpose of this preparatory work is to identify the optimal methods of defining a population at risk and the corresponding reference group in the event of an incident. Depending on the estimated likelihood of the event, some preliminary estimates may be prepared beforehand (by using GIS, for example).

Developing the population register and follow-up

Four activities are required to develop a population register. The first is the identification of the criteria and methods for selecting the subjects (exposed and reference populations). This includes precisely defining the at-risk and reference populations, and listing the possible (practical) sampling schemes and corresponding sample frames. The feasibility and ethical aspects of following up a sample of the exposed (instead of the whole exposed population) should be considered. Sample size estimates can be calculated according to expected health outcomes.

The second task is the preparation of the questionnaire for registering the exposed population, which should ensure unique identification of the individuals. This should ideally be done in advance. The personal identification data should enable the individual data to be linked to those from the population registries (vital statistics, address registry, etc.). Possible constraints due to data protection legislation should be considered.

Third is the identification of the human and technical resources for subject registration immediately following the incident. This should include the feasibility of involving the medical and emergency services in case registration.

The fourth task is the planning of the possible involvement of various institutions in long-term follow-up studies, including the estimation of the human, technical and financial resources needed for data collection, processing and analysis.

Establishing and maintaining the subject register may require long-term organizational, technical and financial support. Its completeness – the inclusion of all subjects according to the register design, the definition of the population at risk, and the inclusion of all follow-up information about the entire population at risk – is crucial to the usefulness of the collected data. The mobility of the population is a main source of concern in long-term follow-up. When migration is related to an incident and to the exposure

or health impact, the lack of full registration leads to biased estimates of the health consequences.

Box 4 summarizes important points about the population at risk.

Box 4. Population at risk – summary

- The health impact assessment must apply to a well defined population. The definition focuses the investigation and enables quantification of the assessments results. Access to demographic information is essential for this task.
- For the optimal use of data sources for rapid determination of the population at risk, the epidemiologist must be familiar with the contents, coverage and accessibility of the data.

Exposure Assessment

General strategy

Exposure assessment within the framework of major chemical incidents has three goals:

- to contribute to quantitative assessment of the health risks to the exposed population;
- to provide exposure estimates for epidemiological studies; and
- to aid in the evaluation of the effectiveness of interventions taken to restrict the emission and dispersion of the contaminants, and to reduce human exposure.

These goals require similar but not identical exposure assessment strategies. This section emphasizes exposure assessment for epidemiological purposes. The limited usefulness of studies on the health consequences of chemical incidents is often due to the lack of appropriate exposure data *(9)*. A substantial investment in exposure assessment is required to ensure better effectiveness of epidemiological follow-up. Present practice shows that the response to a chemical incident must often proceed without a knowledge of the nature and toxicity or even the chemical constituents of the exposure. This can result from a number of factors. Some can be related to delays in characterization of the

pollutants or to limitations in analytical methodology and equipment. Another may be the limited knowledge of the possible toxic properties of the chemicals involved. In such a case, the observed health effects determine the epidemiological approach.

Before making any exposure assessment, it is essential to determine whether a chemical incident is taking place (see Box 5). After confirmation, the first need is to identify the source, if it is not obvious. Contrary to appearances, this may be a difficult task (as in the case of toxic oil syndrome in Spain). Tracing a source in densely industrialized areas poses a particular problem. A notification system that requires all incidents to be immediately reported to an appointed agency may be of benefit.

Box 5. Event in Rotterdam

In September 1994, the emergency response services in Rotterdam were notified of a leaking railway wagon. The wagon's label identified the contents as tetramethyl lead (TML); there was some confusion on the consignment note. The incident caused considerable disturbance, because TML is a highly toxic and volatile chemical for which no direct reading exposure assessment methods were available. After about 1½ hours, the leaking chemical was identified as red wine, which was also the cargo of the two adjacent wagons. The leaking wagon had received a wrong label.

After confirmation, the chemicals involved need to be identified. Here, too, the notification system can be valuable. In some instances, such as releases of a mixture of chemicals, identification can be difficult but should be considered. Fires pose an even more complicated problem, because combustion products also need to be considered, gases can be emitted at high temperature and aerosols with a complex composition may be formed (see Box 6). The feasibility of the assessment of exposure to substances relevant from the health point of view should be considered as well.

The spatial and temporal distribution of the chemical in the environmental medium needs to be determined. Concentrations at various locations and times may depend on the identity and

Box 6. Chemical fire in Basle

In the Schweizerhalle incident (see Annex) over a thousand tonnes of agrochemicals went up in flames, covering a part of the city of Basle with an evil-smelling plume. During the fire, the identities of the burning chemicals were unknown. Even now, the exact composition of the plume to which the population was exposed remains unknown.

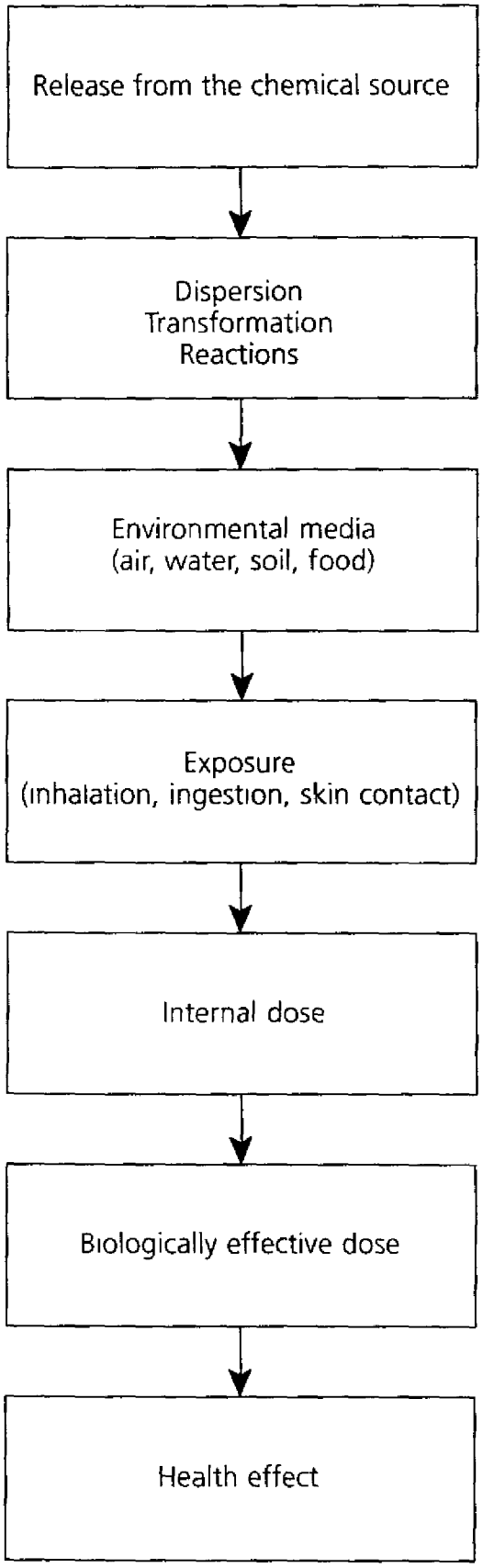
phase (solid, liquid, gas) of the released chemicals. Finally, individual subjects' exposure can be determined by assigning a value to some indicator of exposure. The final two steps of exposure assessment are the main topic of this chapter.

The choice of methods for the exposure assessment must take account of a continuum, from the release of the chemical from its source to the health or nuisance effects it may cause in the population at risk (Fig. 1). At each part of the continuum, different indicators can be identified. These vary between estimates of visible emission or concentrations in media on the one hand to the dose received at a target organ on the other. Their applicability is determined by the validity of the indicators *(10)*, as well as the availability or feasibility of the measurement methods. Conditions after the incident may impose special constraints on method selection.

Almost every observational epidemiological study has to cope with a discrepancy between the ideal (desired) and the attainable exposure data. This discrepancy is even greater in studies of the health consequences of major chemical incidents. The often short duration of the primary exposure, the resultant time constraints and the poor qualitative definition of the toxic chemicals in the acute phase of the incident are particular problems.

More sophisticated indicators usually require more extensive and/or more complex measurement. In most chemical incidents, the biologically effective dose of the toxic chemical cannot be determined. In the few instances where biological monitoring is possible, an internal dose estimate may be feasible. In others, even a clear distinction between exposed and unexposed individuals may be problematic. In the absence of any other measures, however, a surrogate may be used, such as the presence of an individual in a certain exposure zone.

Fig. 1. Source–effect continuum



Different exposure categories
Three different groups of subject may be exposed in a chemical incident:

- emergency response personnel (fire-fighters, rescue workers, police, ambulance personnel);
- personnel from the facility where the incident occurred, including drivers in the case of a transportation incident; and
- the general population, resident and transient.

It is crucial to recognize that these groups may have qualitatively and quantitatively different exposures. For example, soaked clothing may be an additional exposure route and medium for fire-fighters; thus, dermal contact is likely to be more important for them than for the general population. Second, certain sampling techniques may be feasible for one group and impossible for the others.

Primary and secondary exposure
In an incident, a chemical is usually released in one medium: air, water, soil or food. Exposure to this contaminated vehicle is defined as primary exposure. At the incident site, additional exposure media may be involved, such as run-off water used to extinguish a fire. Examples of secondary exposure include ground contamination (exposure via direct contact or the food chain), permeation of drinking-water piping by soil pollutants, food contamination after releases into the atmosphere or deposition in drinking-water or irrigation water. A complicating factor in assessing the exposure caused by the incident can be pre-existing background pollution. Distinguishing this pollution from contamination due to the incident may be difficult.

Exposure assessment methodology
There are three broad categories of exposure assessment: monitoring, questionnaires and interviews, and modelling.

Environmental monitoring estimates the concentrations of the chemical in the environment, biological monitoring estimates the concentrations in exposed humans. Monitoring instruments are used in both cases.

Questionnaires and interviews estimate activity patterns and the location of people during the exposure. A tentative classification

of subjects into exposure categories may result from this information. Acute symptoms may give an indication of the level of exposure.

With exposure models, the concentrations of the chemical in the exposure medium can be estimated without monitoring data. Any modelling attempt should include at least source description, dispersion modelling and exposure modelling. In addition, the observation of vegetation change and the health of animals is a very important indirect method of exposure assessment. Ad hoc inquiries on the health and behaviour of domestic animals may be advisable. In Seveso (see Annex), the first signals of potential risk to human health were the deaths of animals and vegetation.

Often, more than one exposure assessment approach is applied. Even scarce monitoring results may be very useful to verify and adjust model predictions of concentrations. Alternatively, personal monitoring results from a few subjects, combined with questionnaire data, can be used as a basis for the exposure estimates for the population.

Preparedness Phase

The exposure assessment or environment monitoring specialist will make most of the preparations performed. In an emergency, people should be allocated tasks that are related to their regular professional activities. The epidemiologist must consider the following, although other specialists may be responsible for or authorized to implement the relevant activities:

1. preparing for environmental and biological concentration measurements (sampling equipment, sampling teams, system for quality assurance and control);
2. preparing a list of external institutions and experts to supply additional sampling equipment, analytical capability and expertise;
3. securing quantitative information on the storage of chemicals in a locality;
4. identifying any sources of information on background levels of chemical contaminants in the environment and the population;
5. formulating realistic scenarios as an input to exposure models;

6. preparing a system that ensures access for the epidemiologist to exposure-related data (the description of the cause of the incident, the chemicals involved and all data produced by exposure modelling and/or measurements); and
7. identifying the means to design, print and distribute questionnaires.

Response phase

The limited duration of the response phase demands that any attempt to assess the exposure is planned and the necessary personnel trained in advance. There will be no opportunity to replicate a missed or faulty measurement. Accurate and comprehensive exposure data collected in this phase are invaluable, and a recording of the progress of the incident (recording images on video and meteorological data by other means) can be used at a later stage to supplement the measurements.

Exposure monitoring

Exposure monitoring provides the epidemiologist with quantitative data on exposure levels. A monitoring strategy should account for the spatial and temporal variability of the chemicals and their concentrations. As mentioned, two general approaches to exposure monitoring are used: one is based on physical and chemical measurements in the environmental media (environmental monitoring) and the other on measurements of changes in human biological systems (biological monitoring).

Environmental monitoring consists of determining a chemical's concentration in an exposure medium, such as air, water or food. When a single chemical is involved in the incident, rapid identification of the chemical and specific sampling and analysis may prevent waste of monitoring capability. Fires pose special problems because they produce many insufficiently specified chemicals.

In an incident, rescue teams may use direct readout devices for gas measurement to evaluate whether it is safe to enter the hazardous area. The results of these tests should be routinely recorded.

Routine air quality monitoring is usually bound to a fixed location. If additional monitoring sites are identified for use in case of an incident, they should be chosen with a representative

population exposure in mind. Samples can be collected from different environments (both outdoor and indoor) for later analysis; they should be taken at regular intervals if continuous monitoring is not available.

A more direct method of determining individual exposure is to collect personal samples. The feasibility of personal monitoring of the primary exposure of the general population is largely determined by the duration of the exposure, access to the exposed area and practical constraints, such as the availability of monitoring devices (as chemicals often are not specified) and the organization of monitor distribution, collection and registration. Personal sampling of all exposed emergency response personnel is a realistic possibility, and should be considered whenever practicable. Items of contaminated clothing should be sent for analysis. Bioindicators (concentrations of a chemical or its metabolite in plants or animals) are potential signals of environmental contamination and can be useful for human exposure assessment.

An atmospheric emission may last for minutes or hours, but events such as chemical fires can last for days. The composition of the chemicals and their concentrations in the plume may vary with time. Timely and repeated measurements should therefore be made throughout the duration of the release.

Biological monitoring of exposure refers to cellular, biochemical or molecular measures (biomarkers) that are obtained from biological media such as human tissues, cells or fluids and are indicative of exposure to environmental contaminants *(11)*. Its objective is to determine the internal dose or, ideally, the biologically effective dose of the chemical. These biomarkers may consist of concentrations of the parent compound or its metabolites *(12)*. The field of biological markers is still in early stage of development. Only a few valid biological markers are available for epidemiological purposes, in terms of both assessing population exposure and contributing to the quantitative risk assessment. Nevertheless, biomarkers have a number of appealing features. Table 1 summarizes some advantages of and problems with the application of biomarkers of exposure.

Considering the potential of biological markers, every opportunity should be taken to obtain blood and urine specimens from exposed workers and members of the affected population. The personal characteristics of the sample donor, a characterization

Table 1. Advantages of and problems with biomarkers of exposure

Advantages	Problems
They integrate all exposure routes	They may not be chemical-specific.
They can be the only measure of primary exposure, in the absence of environmental data.	They are sensitive to collection and storage methods.
They can assess the effectiveness of protective equipment.	Analysis method may not be available.
They allow for the influence of physical exercise on the inhalation of chemicals.	Sampling strategy must account for the toxicokinetics and toxicodynamics of the chemical.
	Sampling and analysis strategies may have been validated only for occupational exposure
	The chemical to be determined may have a substantial background level.

of his or her possible exposure and the time and location of the sample collection should be recorded. The choice of containers will depend on the requirements of the laboratories involved, but bottles used in hospitals may be suitable, such as EDTA tubes for blood specimens (for testing for heavy metals, pesticides and solvents, for example) and universal containers (plain bottles) for urine samples (for testing for solvents, for example). Specimens should be stored under refrigeration, as directed by the laboratory, and the analysis should be undertaken by laboratories participating in a quality control scheme.

It can be difficult to interpret the results of biological monitoring when the background levels of the biomarkers for the population involved have not been studied previously.

In addition to personal samples from the members of the population at risk, emergency response personnel can be requested routinely to deliver a biological sample after termination of their work shifts. In the event of a controlled evacuation, the collection of biological specimens may be easier if evacuees are accommodated in centralized facilities.

A quality assurance and quality control programme should be instituted whenever environmental and/or biological samples are collected. The topics to be covered are:

- collection (the choice of containers and the possibility of their contamination, type of additives, qualification of personnel, registration of collection time);
- storage and transport;
- the qualifications of laboratory personnel;
- the validity of sampling and analysis techniques for the particular circumstances; and
- duplicate sample collection.

Special attention is needed in cases where more than one sampling and analytical technique has been applied by more than one provider (own personnel, industry, etc.).

Questionnaires and interviews

Questionnaires and structured interviews are used to obtain information from individuals on exposures, factors that may modify their exposure and dose, and/or health effects. Questions related to exposure assessment should therefore be an integral part of any questionnaire to be filled out by the potentially exposed subjects. For the purpose of exposure assessments, the topics covered should at least include:

- activities and whereabouts or locations during the period under study;
- physical activity;
- measures that alter exposure, such as staying indoors or outdoors;
- observations of exposure (sight, smell, taste, etc.); and
- consumption patterns in case of food or drinking-water contamination.

In most emergencies, specially hired staff conduct the interviews. The use of computerized questionnaires and the direct entry of the responses will speed up data processing and the analysis and presentation of the results. Several computer packages can be used for this purpose, including EpiInfo *(13)*.

Exposure modelling

The strength of the modelling approach is that it can make predictions of exposure available to the emergency services within minutes of reporting of the incident. The disadvantage is that

models can only give approximate estimates of dense gas concentration. At present, they do not take account of topography and the built environment.

Exposure modelling must include at least the three phases of source description, chemical dispersion and exposure.

The source description should describe the chemical involved and its physical properties, the release rate and/or total quantity released, and the initial source geometry. Very often the source term (the quantity released) is unknown during the response phase. For example, in the Seveso incident (see Annex), determining which toxic compound was of concern took ten days, and the quantity released is still a matter of dispute *(14)*.

The identity of the chemical and its release rate have to be obtained from the company involved in the incident or after special sampling at the chemical plant. The dispersion of the released chemical in ambient air is determined by the speed and direction of the wind, the buoyancy of the plume, atmospheric stability, the roughness of the terrain (including obstacles) and the physical state of the released material. Modelling exposure involves linking people's location and exposure-relevant behaviour to the concentrations modelled in the previous step. This requires additional data, usually obtained with questionnaires, such as time–activity patterns, sheltering, protective equipment, etc.

Follow-up phase

Assessing primary exposure immediately after the incident is crucial for the follow-up evaluation. The follow-up phase includes a retrospective assessment of initial exposure and the assessment of continuing exposure risk.

Possibilities for retrospective assessment of initial exposure include:

- analysis of all collected environmental samples (using methods with a lower detection limit and/or higher precision, and analysis for additional chemicals), including opportunities for further in-depth investigation of environmental samples such as soil, vegetation or water, which can be used as indirect indicators for human exposure;
- biological monitoring of human beings, in which possible continuing exposure should be considered; and

- post-hoc modelling, in which the estimates of exposure can be further refined because:
  - the quantity released can be estimated more precisely;
  - environmental measurements can be used as an additional input;
  - the boundaries of affected vegetation can give an indication of the amount of chemical deposited; and
  - more sophisticated models can be applied.

In the follow-up phase, banks of biological specimens can give an accurate estimate of exposure. Once samples have been obtained, it may be advisable not to use all the collected material for analysis.

The storage of biological specimens in banks may have a number of advantages *(9,15)*. For example, it permits the analysis of selected samples, such as those from the subjects who will enter a follow-up study, rather than the examination of all specimens, which is usually very costly. New analytical techniques and theories of toxicodynamic mechanisms may develop that may be applied to specimens in existing banks. Finally, specimens stored in banks provide data on the exposure related to the incident.

Box 7 summarizes important points related to exposure assessment.

Box 7. Exposure assessment – summary

- Appropriate exposure data are crucial for studies on the health impact of chemical incidents.
- Individual exposures in the population can be estimated through a combination of static and personal sampling, supported by the use of questionnaires.
- The combination of data collected by modelling and those collected by actual measurement of exposure can improve the accuracy of the estimation of exposure.
- The use of biomarkers to estimate exposure should always be considered.
- Observations by smell and taste, for example, during or shortly after exposure can give an indication of the exposure
- The exposure assessment team should be an integral part of an emergency response team, and requires good organization, equipment, communication and training.
- Exposure monitoring is a continuing task in the follow-up phase.

Health Assessment

Introduction

In this report, health assessment includes the evaluation of the health status of a population exposed to a chemical incident (in different exposure categories, if feasible) and its comparison with the health status of a nonexposed population. A health assessment related to a chemical incident has five objectives:

1. to identify the populations for which action is necessary to mitigate present or prevent later adverse health effects, which includes appropriate treatment for acute, intermediate or chronic health effects;
2. to evaluate the public health implications of the chemical incident, which may include an initial assessment in the response phase and follow-up of exposed people;
3. to evaluate the effectiveness of intervention to prevent exposure and health impairment;
4. to gather knowledge from the incident, through experience of epidemiological studies, which can help in preparedness for future incidents; and
5. to contribute to the scientific knowledge on the toxic properties of certain chemicals and the risk they pose to human beings and the environment.

Health outcome

In some chemical incidents the health consequences are obvious; in others only complex and often lengthy investigations reveal the effects. Incidents of the first type may be recognized immediately, sometimes before any health effects are linked with a chemical exposure. Both Minamata disease *(16,17)* and toxic oil syndrome *(18)* were initially thought to have infectious causes. Even in cases with obvious causality, however, it is important to recognize that the possibility of later effects might be overlooked in the first period, when the focus is on treatment of acute cases. In the second type, the chemical incident may not be perceived, but ill health effects clustered in time and space are recognized by surveillance systems or public awareness.

In outbreaks of toxic illness, it is essential first to confirm that an epidemic of an unusual disease is occurring and second to distinguish this from commonly occurring diseases. The incidental

exposure, however, may increase the incidence of a common disease; this was the case with asthma following exposure to soya bean dust in Barcelona *(19)*. In addition, investigators sometimes find that extensive misclassification of cases has occurred in epidemics of non-infectious disease. In a recent outbreak of optic and peripheral neuropathy in Cuba, patients with a variety of similar but ordinary neurological and psychological conditions were mistakenly included in the case registers, thereby substantially inflating the epidemic curve (P. Baxter, personal communication, 1996). It is essential for clinicians and epidemiologists to agree on the diagnostic criteria for the disease of interest, whether it is present in an outbreak or may arise as a consequence of the toxic exposure. This is important for clinicians managing and treating the cases, as well as for ensuring that misclassification does not lead to bias or weakening of associations in epidemiological studies. The diagnostic criteria on which the case definitions are based may be clinical or a combination of clinical, laboratory and pathological findings.

As in infectious disease outbreaks, the identification of the index cases should lead to screening of the population to identify suspected cases, followed by rigorous investigation to confirm or refute the diagnosis in accordance with the agreed case definitions. Other WHO publications *(1,20)* give further information on investigating diseases of suspected chemical etiology.

To appreciate the full range of health consequences of an obvious chemical incident, in-depth and sometimes long-term investigations and surveillance systems have to be designed and implemented. The identification of acute effects is required for the allocation of technical and social support services, treatment and rehabilitation and for the planning of further investigations. The surveillance of chronic effects completes the health impact assessment (allowing the evaluation of post-emergency measures) and (along with the environmental investigations) may indicate a continuing health risk.

The following categories of health outcome should be taken into consideration:

- toxic effects
- stress-related effects
- effects resulting from a combination of the two.