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Assessing the health consequences of major chemical incidents – epidemiological approaches
Assessing the health consequences of major chemical incidents – epidemiological approaches
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## Contents

- **Foreword** ................................................................. vii
- **Preface** ........................................................................ ix
- **Contributors** .............................................................. xiii

### Introduction: definition and health effects of chemical incidents
- Definition ................................................................. 1
- Routes of exposure ....................................................... 1
- Health outcomes of chemical disasters ....................... 2
- Factors determining and modifying health impairment ........ 3
- Need for systematic health risk assessment ................. 5
- Structure of this publication ........................................ 5

### 1 Role of epidemiology in assessing health effects following a major chemical incident
- Why to employ the epidemiological approach ............. 7
- When a health risk assessment is needed ...................... 8
- Whether to conduct a study – ethical issues ................. 10
- Roles of epidemiology in the phases of incident evaluation .................................................. 11

### 2 Epidemiological tools
- Introduction ............................................................... 19
- Population at risk ......................................................... 19
- Exposure assessment .................................................. 24
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preparedness phase</td>
<td>29</td>
</tr>
<tr>
<td>Health assessment</td>
<td>36</td>
</tr>
<tr>
<td>3 Supportive action</td>
<td>57</td>
</tr>
<tr>
<td>Cooperation</td>
<td>57</td>
</tr>
<tr>
<td>Dissemination of information</td>
<td>60</td>
</tr>
<tr>
<td>Training</td>
<td>66</td>
</tr>
<tr>
<td>References</td>
<td>69</td>
</tr>
<tr>
<td>Annex: summaries of selected incidents</td>
<td>73</td>
</tr>
<tr>
<td>The environmental accident at Schweizerhalle</td>
<td>73</td>
</tr>
<tr>
<td>The Seveso accident</td>
<td>78</td>
</tr>
<tr>
<td>The Shetland oil spill</td>
<td>81</td>
</tr>
<tr>
<td>Toxic oil syndrome in Spain</td>
<td>84</td>
</tr>
<tr>
<td>References</td>
<td>89</td>
</tr>
</tbody>
</table>
Foreword

Chemical incidents can have serious and widespread effects on health. Epidemiology is an important tool for evaluating these effects and thus supplying information on which to base action to deal with a current incident and to help prepare for future ones. Such action helps to create environments conducive to health, which is one of the primary goals of the WHO European strategy for health for all.

Epidemiologists can make a valuable contribution to each phase of a chemical incident: preparedness, response and follow-up. Recognizing this, the WHO European Centre for Environment and Health convened a working group to discuss and set out some of the most effective epidemiological approaches to chemical incidents. This book is the result of the group’s work.

This publication aims to promote awareness of the role of epidemiology in the management of chemical incidents. It identifies the special part that epidemiology can play in a coordinated multidisciplinary response to a chemical incident, the tools to use in health risk assessment and roles in supportive activities such as training and the dissemination of information. The book supports and illustrates its arguments with examples showing the contributions of epidemiology to the management of four major incidents in Europe: the fire at Schweizerhalle, the Seveso accident, the grounding of an oil tanker in Scotland and the toxic oil syndrome in Spain.

Realizing the potential contribution of epidemiology to the management of chemical incidents is an important step in creating an effective multidisciplinary response. Such a response could help to protect health by offering better assistance to people exposed to current incidents and improving preparedness for future events.

J.E. Asvall
WHO Regional Director for Europe
The rapid industrialization of the last two centuries has often caused environmental contamination far beyond the confines of the industrial sector. Further, as the size and scale of industrial activities have increased, a number of dramatic industrial accidents, such as those at Seveso and Bhopal, have heightened public awareness of the potential risks of such activities to the health of the surrounding population and to the environment. Public concern is more acute when the nature and toxicity of the chemicals discharged are uncertain, the extent of environmental contamination is unknown, and the health consequences are poorly understood. Exposure to chemicals may cause new, previously observed diseases or exacerbate diseases of another etiology.

Epidemiology is an important tool for evaluating the health consequences for populations exposed to chemicals as a result of chemical incidents or environmental contamination. Many parallels can be drawn with the use of classical epidemiology in the investigation of infectious diseases. Further, epidemiological methods may be used to evaluate the effectiveness of activities to reduce the health effects of exposure to chemicals.

The participants in the United Nations Conference on Environment and Development, held in Rio de Janeiro in June 1992, noted that gross chemical contamination of the environment with grave damage to human health, genetic material and reproductive outcomes has arisen in recent times in some of the world’s most important industrial areas. They defined an international strategy for the environmentally sound management of chemicals within the principles of sustainable development and improved quality of life for humankind. The participants recognized, however, that both national and international efforts need significant strengthening to carry out this strategy. They identified
the promotion of international cooperation in the prevention of and response to chemical accidents as an important aspect of the process.

Over the past 15 years, both the WHO Regional Office for Europe and the International Programme on Chemical Safety (IPCS) (a joint venture of WHO, the International Labour Organisation (ILO) and the United Nations Environment Programme (UNEP)) have taken a number of important initiatives in the prevention of and response to chemical accidents. Planning emergency response systems for chemical accidents \(^1\) was issued in 1981. In 1987, jointly with the International Council of Scientific Unions (ICSU) Scientific Committee on Problems of the Environment (SCOPE), IPCS published Methods for assessing and reducing injury from chemical accidents. \(^2\) In 1994, IPCS and the WHO European Centre for Environment and Health collaborated with the Organisation for Economic Co-operation and Development (OECD) and UNEP on Health aspects of chemical accidents, \(^3\) giving guidance on chemical accident awareness, preparedness and response for health professionals and emergency response personnel. At present, IPCS is developing guidelines on the role of the public health sector in chemical incident preparedness, response and follow-up, directed specifically at public health policy-makers to help them establish the necessary administrative infrastructure and measures. These guidelines do not deal with the technical aspects and the tools involved, but recognize the need for specific publications on these topics, such as epidemiological methods.

This publication complements those already cited and is directed specifically at the public health official or epidemiologist who may need to plan or undertake an epidemiological study of populations exposed to chemicals through major accidents or environmental contamination. It is meant to promote awareness of the role of epidemiology among public health professionals managing chemical incidents and to describe some tools for


designing and implementing studies, but not to be a detailed technical manual.

After an initial consultation in 1994 and discussion on the need for such a publication at the forum of the European Concerted Action “Air Pollution Epidemiology”, the WHO European Centre for Environment and Health set up the Working Group on Epidemiological Approaches to Assessment of Health Consequences of Accidents and Disasters. At its first meeting in Basle on 12–13 January 1995, the Group examined the epidemiological investigations that had followed a number of well known chemical accidents, to identify the key elements of these investigations as the basis for a guideline document. The Group drew up the outline of the present publication and assigned the sections to be drafted to various experts. The Working Group examined the first draft of the document at a meeting in Bilthoven on 4–5 May 1995. The Editorial Group edited the draft and circulated it for peer review. A summary was presented for discussion at the annual Meeting of the International Society for Environmental Epidemiology in August 1995. As a result of this discussion, and using comments on the draft from the Working Group members and the invited reviewers, the Editorial Group prepared a final version that was reviewed again by the members of the Working Group.

This work was made possible through the financial support of the Government of Switzerland, which is gratefully acknowledged.

I believe that the Working Group has created a good basis for the application of environmental epidemiology to the management of chemical incidents, and that its work will contribute to a reduction of associated health effects.

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Introduction: definition and health effects of chemical incidents

Definition
For the purposes of this publication, the terms “chemical accident” or “chemical incident” refer to an event resulting in the release of a substance or substances hazardous to human health and/or the environment in the short or long term. Such events include fires, explosions, leakages or releases of toxic substances that can cause people illness, injury, disability or death.

The terms accident and incident tend to be used interchangeably. Accident is used most widely to refer to technological failure in a chemical plant or spillage during the transport of a chemical load. The term incident is preferred, because it embraces un-anticipated failures in the integrity of a storage container, as well as events involving human error, sabotage, or social and organizational factors.

Chemical incidents may manifest their presence in one of two ways: a failure in the containment of chemicals, with or without exposure of workers or the population, or an outbreak of illness.

This publication focuses on incidents with a known release of chemicals into the environment. The methodology applied in the investigation of the second type of incident is the subject of an earlier WHO report (1).

Routes of Exposure
Human exposure to chemical releases can occur through air, food and drink, water or direct dermal contact with the chemical. Chemical fires and releases into the air due to failures of production,
storage containers, road and rail tankers or pipelines are the most common incidents involving human exposure. This book therefore focuses on these as the most important public health risks.

Incidents involving drinking-water supplies have not been very important worldwide because most chemical contaminants are readily detectable by smell or taste, and thus people usually avoid drinking water containing them. Foodborne incidents, on the other hand, have given rise to major outbreaks of chemical-induced disease, such as toxic oil syndrome (see Annex) and organic mercury poisoning. Epidemiologists need to be aware that apparently inexplicable disease outbreaks may be the first evidence of a toxic release into the community.

Health Outcomes of Chemical Disasters

Although chemicals have specific modes of action and adverse effects, in most instances the mechanisms and health outcomes of exposure are unknown. In general, the adverse responses to toxic exposures may be:

- effects that are local or arise at the site of contact with the chemical, such as bronchoconstriction from respiratory irritants or irritation of the skin and eyes by irritant gases;
- effects that are systemic or affect organ systems remote from the site of absorption, such as depression of the central nervous system from absorption of solvents through the skin, or necrosis of the liver from the inhalation of carbon tetrachloride; and
- effects on mental health arising from real or perceived releases, which depend on the psychological stress associated with an incident.

Mental effects can arise from disturbing experiences such as traumatic death, or fears of chronic impairment or stigmatization from chemical contamination. Post-traumatic stress disorder, chronic anxiety and depression may be prominent and lead to measurable outcomes. Acute anxiety from the fear of chemical contamination alone can induce physical states that mimic acute, toxic reactions and may lead to diagnostic confusion.

The timing of the adverse health effects after exposure may vary. Acute effects appear within seconds or minutes, and include
eye irritation, bronchoconstriction or pulmonary oedema. Sub-
chronic effects appear within hours or days, and include delayed 
pulmonary oedema from phosgene, or renal failure in arsenic 
poisoning. Chronic effects appear weeks to years after exposure. 
These may be of the greatest concern in an incident, even in the 
absence of any casualties with acute or subchronic effects, and 
may include cancer and reproductive abnormalities.

Chemical-induced disorders can manifest themselves in any 
organ system. Because the body has only a limited repertoire of 
disease responses, the signs and symptoms may resemble dis-
eases arising from other causes. Unless the disorder is highly spe-
cific to the particular agent, epidemiological studies may be nec-
essary to determine whether the occurrence of a disease in a popu-
lation has increased as a result of chemical exposure.

Factors Determining and Modifying 
Health Impairment

In investigations of chemical incidents, the main factors to be 
considered are the toxicity of the chemical and factors influenc-
ing exposure and dose, such as exposure routes, physical charac-
teristics of the chemical(s) involved and the presence of other 
potentiating particles and substances in the release. These may 
lead to heterogeneous effects within the exposed population; 
another important factor is differences in susceptibility between 
individuals.

Toxic effects can depend on the peak levels and the duration 
of exposure, as well as the dose of the chemical. The behaviour 
of individuals following the incident determines exposure and 
dose. For example, extreme fear and lack of preparedness may 
increase exposure to gases by making people flee into the path of 
a gas cloud, hyperventilate, or fail to take the appropriate pro-
tective measures. In the Bhopal disaster, those who ran in re-
sponse to the chaos inhaled larger quantities of methyl isocyanate, 
which caused pulmonary oedema and instant death. The avail-
ability of emergency care should be considered when assessing 
outcomes. For example, the time taken to reach decontamina-
tion or medical facilities may be important. Finally, an inappro-
priate or poorly managed emergency response can become a kind 
of disaster in itself, with psychological and socially disruptive con-
sequences.
Responses in target organs may vary widely in different individuals exposed to the same doses. There are three main mechanisms for differences in susceptibility:

- increased absorption
- increased effects with equally absorbed doses
- lower threshold of effects.

For example, chemicals may be absorbed more readily through the gastrointestinal tract than through the skin, and by children than by adults. Children absorb lead faster through the intestines than through the skin. The newborn have a much higher capacity than adults for percutaneous absorption of lindane from applications of scabicide agents. In the contamination of food and drink, dietary constituents may alter the bioavailability of the chemical.

As to increased effects from equally absorbed doses, people with a slow acetylator phenotype may have a higher probability than others of contracting bladder tumours from carcinogenic aromatic amines. They metabolize a larger proportion of these amines to reactive compounds that induce such tumours.

As to a lower threshold of effects, a pre-existing health condition may reduce the body’s reserve capacity. Well known examples include the sensitivity of asthmatics to exposure to low levels of sulfur dioxide, and that of patients with coronary heart disease to exposure to carbon monoxide. In addition, nutritional deficiencies may increase the risk of toxic reactions.

More examples could be drawn from experience with chemical exposures in occupational settings, but little information is available on individual susceptibility to brief exposures in chemical incidents. For example, human or experimental data are insufficient to allow dogmatism about the likely heterogeneity of effects of single, brief exposures to chemical carcinogens or teratogens. In general, the most susceptible to chemical insults are people at the extreme ends of the age range and those with physiological variants. Such people comprise up to 25% of the total population.

Community vulnerability may be reduced by minimizing the degree of exposure in a chemical incident and influencing individual susceptibility. Socioeconomic or political factors, as well
as housing conditions and nutritional habits common to all communities, should be considered in all phases of chemical incident management.

**Need for Systematic Health Risk Assessment**
In major chemical incidents, the emergency services function as they would in major accidents or fires. The obvious priority is to rescue people, to put an end to the fire or the release of chemicals, and to avoid further casualties, damage and confusion. Firefighters, police officers and ambulance crews all have their assigned tasks and might – in the case of a chemical incident – be exposed while fulfilling their duties. In addition to these activities, however, there is a need to investigate the health impact, pool available data, search the literature, contact outside experts, propose necessary further investigations and advise on preventive measures. An epidemiological team, working within the framework of the emergency response group, can fulfil these tasks.

**Structure of this Publication**
This monograph is arranged in three parts. Chapter 1 addresses the role of epidemiologists in the immediate and longer-term aftermath of a major chemical incident. A rationale and context for employing an epidemiological approach is provided, as well as several recommendations for the proper placement of epidemiological activities vis-à-vis the other vital medical activities that may be required. Chapter 1 also presents important ethical considerations that need to be considered as part of the epidemiological response. Recommended epidemiological activities are described within the three phases of the health assessment: planning and preparedness, acute response and follow-up.

Chapter 2 is intended for epidemiologists and related health professionals participating in the health assessment following a chemical incident. This chapter provides a comprehensive set of practical measures to be taken during the three phases of the health assessment. While a basic familiarity with the terminology, concepts and methods of epidemiology is assumed, the references cited can provide additional study or support for people who will be involved in these health assessments and need further information.
Chapter 3 discusses the need for collaboration between epidemiologists and other professionals participating in a health assessment. It recommends a collaborative, interdisciplinary approach, but does not suggest that epidemiology is any more important than other areas involved in the response. In fact, it is as part of a broad, multidisciplinary approach that epidemiology’s tangible benefits will be observed. Chapter 3 also covers issues related to the communication and dissemination of information resulting from health assessments, and training needs.

Examples illustrating the principles presented in the text are offered wherever possible. Additionally, an Annex is provided, containing several case studies of health assessments following significant chemical incidents. These can only be considered as illustrative, however, since all chemical incidents present unique problems requiring specially tailored responses. In addition, cultural, economical and political circumstances usually influence eventual health assessment strategies.
Role of epidemiology in assessing health effects following a major chemical incident

Why to Employ the Epidemiological Approach

Epidemiology is a “science studying distribution and determinants of diseases in human populations, and applying this study to control of health problems” (2). It is an essential tool for evaluating the health consequences of environmental exposure. The practice of studying populations at risk, monitoring changes in exposure or health status, recording and interpreting data, and following up communities at risk has been adopted by numerous groups, including environmental and health policymakers. The past decades have seen rapid advances in methods of exposure assessment, health data collection, information management and statistical analysis. These perspectives and methods can be of great practical value when assessing a community’s health after an accidental exposure to one or more potentially toxic substances.

Management of a chemical incident involves decisions on re-location, medical treatment or other actions. These decisions must be based on reliable and timely information. In the event of a major chemical incident, epidemiology has a central role in gathering the information needed to undertake the health risk assessment and providing accurate and timely advice to emergency officials and to the population at risk.

The vast majority of chemicals in use today have not been adequately investigated for their impact on human health at doses
that can be received following an accidental release. Chemical incidents may be complicated by fires or chemical reactions producing mixtures of chemicals, and these may have effects over and above those anticipated by exposure to the individual substances alone. The toxicology of the products of the reactions is often not well understood. Thus, without appropriate expert guidance, public health officials will rarely be able quickly and accurately to determine the range of potential short-term and long-term adverse health effects, the expected severity of these effects, and their frequency (the proportion of the exposed population estimated to be affected). For these reasons, the full participation of an epidemiologist, from the beginning of the work of the emergency response team and including the preparedness for the incident, should result in a more accurate and comprehensive health risk assessment.

Epidemiology has an essential public health role in devising and evaluating intervention measures taken to prevent the worst consequences of an incident. This role is best accomplished by a team that includes toxicologists, exposure assessment specialists and public health officials or managers.

**When a Health Risk Assessment is Needed**

A rapid health risk assessment is needed in all incidents, so specialists with experience in doing such appraisal should always be available as members of the emergency team. Health risk assessments are essential to ensure that the health needs of the population are met, even in minor incidents that do not seem to jeopardize physical health. In some incidents, psychological stress may far outweigh physical risk from chemical exposure; reducing the level of anxiety in the community may be the main justification for an assessment.

In the event of an outbreak of illness or a severe incident involving fatalities, there may be little doubt about the need to establish the chemical agents and their effects. Other incidents may result in few, if any, immediate casualties, but medical and public concern may focus on the potential for long-term effects, such as carcinogenicity or teratogenicity. In-depth follow-up studies will be needed to confirm or allay these anxieties.

Epidemiological and clinical studies after chemical incidents will have two main purposes:
ROLE OF EPIDEMIOLOGY

- scientific (to measure the morbidity and mortality associated with the chemical exposure as part of the health risk assessment); and
- case finding (to detect treatable disorders associated with the chemical exposure or to provide reassurance).

Unfortunately, no formula can be provided for determining whether an in-depth assessment involving special resources should be undertaken. The following need to be taken into account:

- uncertainty about the extent and severity of the exposure
- uncertainty about the toxic hazard and likely health effects
- the community’s perception of health risk
- ethical considerations
- liability issues.

Accidental chemical exposures have sometimes been ignored, from the health standpoint, for months or years after the event (see Box 1). The problems associated with the management of the example given illustrate the importance of contacting and registering exposed people as soon as possible, and obtaining immediate objective exposure data as well as environmental samples. Retrospective health assessments have proved to have a very limited ability to provide a comprehensive and accurate picture of an accident’s impact on human health.

Box 1. The northern Cornwall incident

In an incident involving water contamination by aluminium sulfate in northern Cornwall, United Kingdom in 1988, failure to carry out rapid epidemiological assessment contributed significantly to psychological stress among the population. A retrospective investigation found an increased incidence of a wide range of symptoms in people who were exposed, but researchers could not exclude the possibility that these associations were due to anxiety and the publicity associated with the incident. Further, the overall response rate was low. This was attributed to “confusion about planned long-term studies and other studies set up by local interest groups”, and delay in conducting the survey (3,4).
Ideally, the decision about whether to initiate a health assessment should be heavily influenced by a team of scientists, including one or more epidemiologists. Depending on the incident, the team should include one or more public health physicians, toxicologists, environmental engineers (such as hydrogeologists) and government officials. Additional technical support may be required from such diverse professionals as microbiologists, occupational hygienists, agricultural scientists and veterinarians. The active participation of representatives of the affected community and of interest groups may facilitate decision-making. Such people, however, may over- or underestimate the significance of the episode and be biased in their opinions on the need for further studies.

Finally, whether it is decided to go forward with a detailed health assessment or not, the reasons for the decision must be set down in writing and kept for future use. The document should be shared with individuals and organizations wanting to know the rationale for the decision.

**Whether to Conduct a Study – Ethical Issues**

Considering the technical issues in planning the study related to the incident, as described above, an epidemiologist must remember the basic ethical principles of beneficence, non-maleficence, justice and autonomy governing the conduct of any health-related investigation. Important issues to consider include informed consent, the guarding of privacy, peer review and the dissemination of results. In the case of environmental incidents, conflicts of interest might arise among various interest groups (such as industry, the local community, the local administration and researchers) and individuals within the community. Some conflicts may influence the results of an investigation assessing the health consequences of the incident. When strict diagnostic criteria are not applied, people may either expect a return (such as compensation) or be disturbed by the idea of being labelled as contaminated. Further, bias in reporting symptoms is common, and pressure from individuals and scientific uncertainties may modify physicians’ sensitivity and specificity in identifying victims of the accident, particularly in borderline cases.

Epidemiologists are often pressed to quantify the consequences of an incident quickly. The zeal of John Snow, who produced his
report on the Broad Street pump in little over three months, should be in the forefront of the epidemiologist’s mind (5). Nevertheless, before launching any study, consideration should be given to a number of critical questions, such as those given in Box 2. Local or national committees on research ethics may help answer such questions.

**Box 2. Ethical considerations in a decision to undertake a study**

1. Might the desire for a more scientifically complete study unduly delay the implementation of preventive measures?
2. Has the proposed research programme been thought through sufficiently to be put down on paper?
3. Could the retrieval of information on exposure and/or outcome compromise people’s privacy? If so, how should the investigators interrelate with those investigated?
4. Is it possible to predict whether the results will lead to excessive use of medication and medical services?
5. Will the survey uncover conditions not amenable to treatment? If so, will the community still agree to participate in the study?
6. Could the study itself or its predictable findings lead to undue discrimination, for example, following the registration for clinical purposes of all those exposed?
7. Have potential conflicts of interest between sponsors, investigators and study subjects been disclosed?
8. Will the study subjects receive an explanation adequate to ensure that their consent to participate will actually be informed?
9. Will the study create anxiety disproportional to the foreseeable benefits?

**Roles of Epidemiology in the Phases of Incident Evaluation**

The three chronological stages of the evaluation and management of a chemical accident are called the planning and preparedness phase, the response phase and the follow-up phase.

**Planning and preparedness**

The preparedness phase takes place during the period before a chemical release. In practice, it is a continuous activity, with
periodic updates and revisions. This is the time to prepare an efficient and effective system for emergency response (incident management), rehabilitation and follow-up.

Activities in this phase include:

1. establishing and maintaining an inventory of potential risk sources, such as hazardous installations and transport routes;
2. establishing a chain of command and a network of cooperating emergency response services and expert consultants;
3. drafting emergency response guidelines and medical treatment protocols;
4. running collaborative (interagency) training sessions with every party involved in the emergency response;
5. obtaining all necessary equipment and supplies, or making arrangements to obtain them at short notice in case of an emergency; and
6. planning for an emergency under existing legislation with industry and local authorities.

Role of epidemiology
During this phase, an efficient and effective system should be prepared for initiating an emergency response and planning rehabilitation and follow-up. Adequate resources should be dedicated to this task. In this period the decisions can be made by consensus. Any activity that can be performed in the response stage should be included in the contingency plans developed in the preparedness phase.

Important stimuli for adjustment of the contingency plans in this phase are the experiences from previous emergency responses and/or training sessions. Specific activities include:

1. identifying the epidemiologist’s role in the planning team;
2. identifying population and health data sources;
3. identifying existing environmental monitoring networks;
4. identifying poison centres active in the area;
5. preparing for the planning and conduct of epidemiological studies;
6. specifying and preparing methods for rapid assessment of potential health effects, including facilities for collection, storage and analysis of biological samples; and
7. testing the methods for investigating disease outbreaks and performing other small surveys of acute incidents.

Response
The response phase starts when it is recognized that an incident has occurred, and lasts as long as rapid interventions are conducted. As quickly as possible and under pressure of time, decisions are made according to the prearranged chain of command, and emergency response personnel attempt to comply with prepared contingency plans.

Activities in this phase include:

1. verifying the incident, and identifying the source and nature of chemical(s) and/or the nature of immediate health consequences;
2. terminating the incident and/or the associated chemical release;
3. preventing exposure to employees, emergency response personnel and the general population;
4. assessing the exposure and health outcomes;
5. assessing health risk to exposed individuals and to the population;
6. preventing and/or mitigating adverse health effects due to exposure, by advising the public and the authorities;
7. providing medical treatment of casualties; and
8. identifying the casualties.

Role of epidemiology
During the response phase, the epidemiologist undertakes health risk assessment, defines the populations at risk of different types of exposure, rapidly collects valid data on health status and exposures, and relates exposure data to information on health status. The epidemiologist should also be involved in evaluating the impact of the incident and, in this way, provide the background for the advice on preventive intervention measures given to the public and public health officials.

Carrying out epidemiological functions during the response phase is often difficult, because many emergency response personnel do not perceive the relevance of field epidemiology at that time. All public health professionals and emergency personnel
must therefore understand the role of epidemiology and the need for data collection during the acute crisis. Epidemiological input in the planning and preparedness phase is essential to achieve this.

Several illustrations of epidemiological activities in the response phase of health assessments exist. For example, during the 1986 incident in Basle (see Annex), epidemiologists analysed daily mortality, inpatient and outpatient attendance and symptoms in different population groups (6). In the Shetland oil spillage in 1993, epidemiologists determined the immediate effects and collected baseline health data and biological measurements (7). The Annex provides some details of these incidents and describes the involvement of epidemiologists in their evaluation.

**Follow-up**
The follow-up phase encompasses the time after the termination of the rapid response activities. It lasts as long as effects of the incident can be expected to occur.

Once the acute phase is over, the general public tends to return to its usual activities, and becomes less interested in the incident or its consequences. In contrast, the people affected by the incident start the process of coping with the consequences. While more time is usually available to make decisions than in the response phase, public and political pressure may place time constraints on studies of health consequences.

Activities in this phase include:

1. rehabilitation, that is, restoring the affected area, its occupants, workforce and emergency response system to a state equivalent to or better than the original;
2. follow-up of exposed employees, emergency response personnel and the general population, including:
   - the provision of medical, social, economic and psychological care;
   - epidemiological follow-up of the incident;
3. risk assessment of the health consequences of the incident;
4. follow-up and/or clean-up on the environmental consequences of the incident, which (from a public health perspective) may cause secondary exposure through, for
example, contamination of the food chain and/or drinking-water; and
5. appraisal of the emergency response phase.

Evaluation of an incident should lead to recommendations to prevent repetition and to adjust emergency response plans where they did not perform perfectly.

Role of epidemiology
In the follow-up phase, health risk assessment should be continued whenever there are reasons to suspect medium- or long-term effects. Such effects may include disturbances of lung function, neurological and behavioural disorders, allergy, adverse pregnancy outcome and cancer. A decision as to whether such adverse effects may be expected must be made promptly, with the collection of baseline data on both exposure and earlier health status commencing as soon as possible. Urgent toxicological expert consultations are usually necessary and should be carried out without delay, for example, by contacting poison information centres. Advice from an occupational health specialist may also be valuable.

Epidemiological follow-up should include the activities listed in Box 3. They may be undertaken:

- to respond to public concern and to alleviate the worries of people exposed in the incident and those living in the vicinity of chemical plants;
- for the purposes of current or future litigation or compensation;
- owing to political pressure to do something;
- to expand knowledge on health effects in exposed populations; or
- to develop evidence of a causal connection between exposures and health effects.

A considerable part of the information needed in the follow-up phase must be collected during the response phase. This should be anticipated during the planning and preparedness phase. Further, in the longer-term aftermath of an incident, official and public interest is likely to wane. It is therefore important for public health authorities at all levels to accept the need to support and
fund follow-up studies, and to build this consideration into the planning and preparedness phase.

**Box 3. Epidemiological activities in the follow-up phase**

These activities include:
- following up cases or the exposed population;
- establishing a study to evaluate long-term health effects;
- evaluating the effectiveness of response action and making recommendations to improve the response; and
- making recommendations to improve existing databases and other sources of information.

Follow-up studies should be carefully designed and implemented in order to overcome particular problems. These problems are related to:

- **population:**
  - size (and its effect on study statistical power); and
  - mobility and cooperation (maintaining high response rate during follow-up);

- **health outcomes:**
  - the unknown (but often long) latent period from exposure to effect;
  - the changing background morbidity of the population over a long time;
  - the need to separate the effects of exposures in multifactorial diseases;
  - the availability of valid and comprehensive data; and
  - possible bias in subjective assessment of health status related to special interests (such as political issues or the prospect of financial compensation);

- **availability of reliable quantitative data on exposure;**

- **technical and feasibility issues:**
  - focus on long-term studies during the acute phase;
  - the need for resources to obtain and store samples and to set up registers in acute situations; and
- the lack of standard definitions, and of measurement tools to use and to permit comparison of studies.

Properly implemented follow-up studies provide unique opportunities to obtain information on the long-term results of exposure to chemical substances. Thus, they should be seriously considered as part of the response to all chemical incidents.
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
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.

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.
Fig. 1. Source–effect continuum

1. Release from the chemical source
2. Dispersion
   Transformation
   Reactions
3. Environmental media
   (air, water, soil, food)
4. Exposure
   (inhalation, ingestion, skin contact)
5. Internal dose
6. Biologically effective dose
7. Health effect
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
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:

Table 1. Advantages of and problems with biomarkers of exposure

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Problems</th>
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<tbody>
<tr>
<td>They integrate all exposure routes.</td>
<td>They may not be chemical-specific.</td>
</tr>
<tr>
<td>They can be the only measure of primary exposure, in the absence of</td>
<td>They are sensitive to collection and storage methods.</td>
</tr>
<tr>
<td>environmental data.</td>
<td></td>
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<tr>
<td>They can assess the effectiveness of protective equipment.</td>
<td>Analysis method may not be available.</td>
</tr>
<tr>
<td>They allow for the influence of physical exercise on the inhalation of</td>
<td>Sampling strategy must account for the toxicokinetics and toxicodynamics</td>
</tr>
<tr>
<td>chemicals.</td>
<td>of the chemical.</td>
</tr>
<tr>
<td></td>
<td>Sampling and analysis strategies may have been validated only for</td>
</tr>
<tr>
<td></td>
<td>occupational exposure.</td>
</tr>
<tr>
<td></td>
<td>The chemical to be determined may have a substantial background level.</td>
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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.
Toxic effects
Toxic effects can be acute, subchronic, chronic or a combination of the three, as in the Seveso incident (see Annex) (14). The caustic dermal lesions in children who were directly exposed to the toxic plume were an acute effect. The chloracne that appeared in the following days in children can be described as a subchronic effect, while the incidence of lymphopoietic cancers a decade after the incident, slightly greater than expected, suggests the existence of a chronic effect.

The latent period before the health consequences become apparent depends on the exposure, the toxicity of the released agent, and the nature and history of the disease process. The persistence of environmental contamination creates a risk of delayed exposure and health effects.

Stress-related effects
Stress-related effects may be mental or physical. Mental consequences not only entail immediate signs such as anxiety, anger and depression but may also find expression months or years later. An example of the possible influence of post-incident stress on physical health is the mortality study in Seveso (21). This demonstrated that the population of the most contaminated area, which had suffered the greatest psychosocial impact of the incident, showed noticeably higher cardiovascular mortality than a comparable population from an area with similar social, environmental and cultural features.

The psychological consequences of a traumatic experience, including acute or chronic exposure to toxic or noxious substances, depend to a large degree on the exposed person’s perception of the severity or danger of the exposure. Despite reassurance, people may interpret incidents involving minor, or even nonexistent human exposure as life threatening. False perceptions of risk may lead to physiological reactions. Post-traumatic stress syndrome after major disasters is a well recognized entity and might mimic toxic illness.

Combination of toxic and stress-related effects
The stress caused by an incident might interact with toxic effects and increase the probability of symptoms or even disease. In this context, it is important to recognize that psychological effects are
health events and that a combination of toxic and stress-related effects might act synergistically.

**Measures of health outcome and strategies for health assessment**

Health outcomes can be measured in different ways. In general, the following health consequences should be considered:

- functional and physiological changes
- morbidity, including physical and psychological symptoms
- mortality.

Table 2 gives some examples of measures of functional and physiological changes, as well as of symptoms, related to different organ systems. In a clinical setting, these measures are used to make a specific diagnosis of health outcome. They can also be employed in epidemiological studies following an incident. Those used will depend on the incident type. If the nature of the incident and the chemicals involved are well established, the set of outcomes studied should be determined by their biological plausibility, clinical significance and relevance to possible scientific investigations following the incident. The clinical tests and questionnaires used for the measurement should be based, whenever possible, on previously validated and standardized protocols.

Few of the measures listed in Table 2 can be readily applied to a population soon after an incident without conducting a special study. Less precise but existing indicators of population health status must be used. These are often based on routine data collection systems (Table 3). Further, indirect measures of health status can be used, such as reports of complaints from a population to emergency services, data on school or work absenteeism, or data on sales of specific medicines in pharmacies. In practice, the following strategies have to be applied in succession to assess the health effects of chemical incidents:

1. collection and interpretation of existing health data; and
2. organization and conduct of special studies (if needed).

To quantify a population’s health status, the health information must be referred to a population at risk and take account of some basic demographic characteristics, such as sex and age.
<table>
<thead>
<tr>
<th>Organs or systems</th>
<th>Health outcomes or related diagnostic tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular system</td>
<td>Blood pressure</td>
</tr>
<tr>
<td></td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td></td>
<td>Serum cholesterol and triglycerides</td>
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<tr>
<td></td>
<td>Fitness testing</td>
</tr>
<tr>
<td></td>
<td>Cardiovascular symptom questionnaire</td>
</tr>
<tr>
<td>Respiratory system</td>
<td>Spirometry (forced expiratory volume in 1 second, forced vital capacity)</td>
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<tr>
<td></td>
<td>Bronchial reactivity testing</td>
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<tr>
<td></td>
<td>Chest X-ray</td>
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<td></td>
<td>Bronchial lavage</td>
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<tr>
<td></td>
<td>Immunological test, such as IgE for sensitizers</td>
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<tr>
<td>Liver</td>
<td>Liver function tests</td>
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<tr>
<td></td>
<td>Serum markers, such as aminotransferases (aspartate aminotransferase, alanine aminotransferase), alkaline</td>
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<tr>
<td></td>
<td>phosphatase, gamma-glutamyl transpeptidase, bilirubin</td>
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<tr>
<td></td>
<td>Ultrasound</td>
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<td></td>
<td>Liver biopsy</td>
</tr>
<tr>
<td>Kidneys</td>
<td>Urinary enzymes and proteins</td>
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<tr>
<td></td>
<td>Plasma urea and creatinine</td>
</tr>
<tr>
<td>Central and peripheral</td>
<td>Batteries of neurobehavioural tests</td>
</tr>
<tr>
<td>nervous systems</td>
<td>Visual evoked potentials and reflex studies</td>
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<td></td>
<td>Electrodiagnostic/nerve conduction studies</td>
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<tr>
<td></td>
<td>Magnetic resonance imaging</td>
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<tr>
<td></td>
<td>Plasmalerythrocyte cholinesterase</td>
</tr>
<tr>
<td>Endocrine system</td>
<td>Thyroxine, 3,5,3-tri-iodothyronine, thyroid-stimulating hormone, luteinizing hormone, follicle-stimulating</td>
</tr>
<tr>
<td></td>
<td>hormone, etc.</td>
</tr>
<tr>
<td>Blood</td>
<td>Full blood count</td>
</tr>
<tr>
<td></td>
<td>Methaemoglobinemia</td>
</tr>
<tr>
<td>Skin</td>
<td>Patch testing</td>
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<tr>
<td></td>
<td>Skin biopsy</td>
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<tr>
<td></td>
<td>Inspection/photograph</td>
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<tr>
<td>Reproductive organs</td>
<td>Epidemiological questionnaires</td>
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<td></td>
<td>Sex ratio</td>
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<td></td>
<td>Sperm counts/morphology and motility</td>
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<td></td>
<td>Birth weight</td>
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<td></td>
<td>Spontaneous abortion</td>
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<td></td>
<td>Stillbirth</td>
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<tr>
<td></td>
<td>Congenital defects</td>
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<tr>
<td></td>
<td>Congenital anomalies</td>
</tr>
<tr>
<td>Mental functioning</td>
<td>General health questionnaire score</td>
</tr>
</tbody>
</table>
### Table 3. Data on disease occurrence in population

<table>
<thead>
<tr>
<th>Type of data</th>
<th>Contents of the data set</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vital statistics</strong></td>
<td>Mortality data</td>
</tr>
<tr>
<td></td>
<td>Birth data</td>
</tr>
<tr>
<td><strong>Routine morbidity statistics</strong></td>
<td>Hospital admissions/discharge data</td>
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<tr>
<td></td>
<td>Data from sentinel general practitioners</td>
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<tr>
<td></td>
<td>Abortion register</td>
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<td></td>
<td>Malformation register</td>
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<td></td>
<td>Cancer register</td>
</tr>
<tr>
<td><strong>Non-routine health data</strong></td>
<td>Data from health studies under way</td>
</tr>
</tbody>
</table>

### Use of existing health data

Epidemiologists need to know about the health data available in the region, their accessibility and their potential for use under the particular circumstances. It must be assumed that the existing data systems are not, in principle, designed for use in emergencies and each of the data types has its advantages and limitations. Combining information from several systems may help to improve the general assessment of the health situation and the impact of the incident on it. The following considerations apply to various types of data.

**Mortality data**

A rapid assessment of death certificates consists of counting the number of deaths recorded daily and comparing it with the expected number of deaths in the population at risk. A later analysis of death certificates indicates whether an increase in mortality has occurred, whether this increase has continued for some time and whether it has been followed by a period of lower mortality. Assessing cause-specific mortality is problematic since health officials aware of the diseases expected in the aftermath of an incident may introduce classification bias.

**Hospital admission data**

The following questions have to be answered about hospital admission data.
1. Does the hospital system relate to a specific area; in other words is there a defined referral practice to a specific hospital for the population living in the same area?

2. Can hospital admission data be related to population?

3. Do all hospitals into which patients might have been admitted take part in the recording system?

4. Do all hospitals admit emergency cases, or are emergencies only admitted to a few and the patients distributed later?

5. Is it possible to detect an immediate or a slow, delayed increase in admissions?

6. Are diagnostic criteria recorded for the patients admitted?

7. Is it possible to recognize a small increase in specific diagnoses?

As with mortality data, it should be remembered that small increases in hospital admissions might be disregarded immediately after the incident; a later analysis of the workload of emergency services and non-elective hospital admissions should be conducted. In the acute phase, it has to be decided whether it is possible to ascertain the casualties from the routine records of the hospitals or emergency wards, or whether a special database has to be created. Combined with information on the place where exposure occurred, these data can be used to map health effects. Later, hospital emergency data, overall or cause-specific admissions, or data from subgroups such as elderly people can be analysed by date of admission.

Data from outpatient services, private practice and other primary care facilities

Many health care systems do not have patient recording practices that identify the date of contact. It might be necessary to request that primary health care facilities specially record all new cases and all patients they see. A communication system for such emergencies has to be established in the health care system. In addition, pharmacies might notice an unusual demand for certain products.

Data from disease registers

Some countries have population registers for specific diseases and congenital anomalies. The most common disease registers are for cancer. They can be very helpful during the follow-up phase and can help identify any long-term consequences. Malformation
registers can be invaluable in identifying increases in birth defect rates. There is, however, a danger that if a teratogenic effect is feared, indications for therapeutic abortions will be broadened, possibly influencing the observed malformation rates. In most countries, statistics will record an increase in abortions. Birth certificates and the analysis of births 6–10 months after the event might give some estimates about increased abortion rates, altered sex ratios, birth weight distribution, etc. If an appropriate data system does not exist, the possibility of creating population-based registers for specific conditions should be considered by an ad hoc committee, including experts in both registration and in the natural history of the condition proposed for registration. In principle, one should be cautious before diverting resources for this purpose if they could be more profitably used for others. If it is decided that a population-based register for a given condition is needed, adequate training of its staff should precede implementation.

Other available data
An incident can disturb a population’s social and occupational activities. In part, this can be due to the somatic or physiological health effects of the incident. Systematically collected data on school or work absenteeism may be used as an indirect indicator of health impact. Other factors besides health reasons, including rescue operations or preventive measures, may influence the normal activities of the population and bias the health assessment made using this indicator.

As to complaints and annoyance, officials should record the numbers of telephone calls of complaint that they receive from the population. These calls can also be used as a qualitative indication of the concerns of the population.

In many countries, health interview surveys are conducted, and provide useful information about the background health status of the population. The results of such surveys may serve as a reference to the observations made after the incident, provided that the methods used were comparable to those routinely employed (22).

Analysis of routinely collected data
Routinely collected data can be analysed in two different ways: by temporal or geographical aggregation. Temporal comparisons
are usually conducted with time–series procedures but, in the case of an incident, the data can also be split into those collected before and after the event for simple analysis.

A cross-sectional (or spatial) analysis of routinely collected data is possible when an incident has a presumably broad geographical impact and the population at risk is large. Splitting the whole study area into different classes of exposure will allow the examination of a dose–response relationship if there are exposure measurements or at least reliable estimates for all geographical units. Data must be available on diagnosis, age, sex and location of residence (by postal code) or place of exposure. Potent confounders in this type of analysis are demographic and socio-economic differences between areas. While these can produce false positive or false negative results, the lack of individual exposure assessment in aggregated register data relying only on geographical criteria will result in random misclassification; this reduces the strength of association of a real effect. Studies using register data to examine incidents with geographically limited impact and with a small population at risk may present negative or no-effect results for rare events such as deaths from or hospital admissions for specific diseases. This can result from the lack of power due to the small number of cases, and difficulty in distinguishing the increase from random variation in the disease incidence.

Organization and conduct of special studies of health effects

Soon after the incident, a framework should be made, determining which health effects ought to be assessed and how. The data sources mentioned above are not alternatives; they should be examined together to draw a complete picture of the health effects. Any collection of new data requires a study protocol that takes account of the important issues of standardization of methods, adequate population selection, study power and data analysis.

A study of the health effects of an incident should include information on exposure. As described in the previous section, this can be obtained from questionnaires or from the collection of biological samples, which provides markers of exposure additional to the exposure indicators gathered through environmental sampling. Standardization and quality control in biological and physiological measurements have to be guaranteed, as in
any epidemiological study. In addition, appropriate control for all relevant confounders must be ensured.

**Screening for prevalent conditions**

The attempt to identify everyone in the exposed population who exhibits conditions related to the incident (and to provide such people with medical care, if believed to be needed) corresponds to the conventional definition of screening (23). After an incident, such screening serves political rather than scientific purposes. The absence of any specific hypothesis or clearly defined endpoints will produce new problems: a variety of health disturbances may be detected, with unknown frequency. It is not easy to assess whether an association with the incident exists, and whether any such association is causal; this is difficult to explain to the exposed population and to the political authorities.

Screening focused on specific conditions may be reasonable, if based on a plausible hypothesis. Nevertheless, screening programmes have the same basic principles, potential and limitations after an environmental incident as in any other circumstances. In spite of the chaos that often follows such an event, the basic rules for any screening programme (Box 8) should therefore be kept in mind.

---

**Box 8. Rules for a screening programme**

*The people involved in any screening programme should:*

1. plan procedures for the recruitment of each individual of the population to be screened;
2. periodically estimate the extent of participation and make inquiries to determine the reasons for non-response;
3. be aware of the sensitivity and the specificity of the diagnostic test used;
4. design a protocol for subsequent, more refined, diagnostic procedures (when needed) and the administration of therapy (if required);
5. identify an epidemiologist to be responsible for the programme and ensure coordination with participating clinicians;
6. estimate the expected effectiveness and efficacy of the programme; and
7. make sure that adequate treatment facilities are available for all cases found.
Short- and long-term screening programmes that do not adhere to these principles may do more harm than good. Unnecessary medical examinations or laboratory analyses are a waste of resources and prevent delivery to all the population of procedures that are actually needed.

Once the decision to implement a particular screening programme has been made, it can be used to estimate the prevalence of the condition being investigated. The distinction between screening and prevalence estimation should be borne in mind: screening implies approaching each member of the population while prevalence can be estimated using a sample. If participation in the screening programme is lower than 100%, selection bias may affect estimates of prevalence.

Study designs
The challenge for environmental epidemiology is to link exposure to health data. The section on exposure assessment addressed the possible options and difficulties involved in each part of a study. Health effects can be assessed using routinely collected data (see Table 3) or by conducting special studies. These can be classified according to the general principles of epidemiology into descriptive and analytic studies (see Tables 4 and 5). Descriptive studies use exposure or health data gained from different existing sources and identify differences in health outcomes in discrete exposure groups.

The availability of existing data determines the type of descriptive study to conduct. In contrast, in analytical studies, data collection is determined by the study design selected: the one considered to be optimal for theoretical and practical reasons in a particular post-incident situation. The analytical study is conducted in study groups specially selected for the purpose.

In the planning of a special study on health effects, a central issue is the question of adequate selection of populations to be studied and the requisite health outcome definition. Table 2 provides some examples of target organs and health measures that could be studied. Usually, physiological or functional measurements are combined with questionnaire data. It is important to be aware of existing questionnaires and to be able to adapt them to the situation as quickly as possible. To do so, the epidemiologists involved need to have access to validated questionnaires on symptoms for different organs or systems, when they exist. A
Table 4. Linking health and exposure data through descriptive studies

<table>
<thead>
<tr>
<th>Health data</th>
<th>Exposure data</th>
<th>Study design</th>
<th>Analysis</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms and signs in the population</td>
<td>Individual, qualitative</td>
<td>Survey/ cross-sectional</td>
<td>Comparison of different exposure groups</td>
<td>Frequency of symptoms (including annoyance/ anxiety) in different exposure groups</td>
</tr>
<tr>
<td>Biological measurements</td>
<td>Individual, qualitative and/or quantitative</td>
<td>Cross-sectional (random sample or cluster sample)</td>
<td>Comparison of different exposure groups</td>
<td>Correlation between markers of health effects and markers of exposure</td>
</tr>
<tr>
<td>Disease occurrence</td>
<td>Population-wide</td>
<td>Temporal aggregation</td>
<td>Time-series</td>
<td>Change in rates</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Spatial aggregation</td>
<td>Spatial comparisons</td>
<td>Difference between areas exposed and not exposed</td>
</tr>
<tr>
<td>Mortality, birth weight, etc.</td>
<td>Population-wide</td>
<td>Temporal aggregation</td>
<td>Time-series</td>
<td>Short-term changes in mortality, birth weight, etc.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Spatial aggregation</td>
<td>Spatial comparisons</td>
<td>Difference between exposure groups</td>
</tr>
</tbody>
</table>

Publication of European Concerted Action “Air Pollution Epidemiology” (24) gives an overview of symptom questionnaires for respiratory effects. Less standardization exists in the assessment of neurological symptoms. Other common health symptoms (such as headache, sickness and vomiting) may be measured in population surveys on general health status.

Further, a study of health effects should measure the psychological impact of the incident. As mentioned, anxiety or stress can be considered adverse health effects or as effect modifiers when somatic symptoms are considered.
The collection of data on functional, physiological and other objectively detected changes in health requires a special study. Well standardized methods for population studies of lung function or bronchial reactivity exist and have been tested in various epidemiological studies (25,26). The same is true for neurological effects or other systemic effects. In Seveso (see Annex), clearly defined criteria were used to diagnose skin effects (27).

Analytical studies

The usual classification of analytical study designs in environmental epidemiology include panel, cohort and case-control (case-reference) studies (28). In assessing an environmental incident, these study types are not clearly different; a panel study would follow the groups selected from the at-risk and reference populations, and would then be later integrated into a cohort study. A descriptive study can identify cases or exposed groups and provide the basis for an analytical study.
Panel studies are used for the short-term follow-up of a group of people whose health and exposure are closely monitored. The health data may be collected as repeated measurements of health events (a few times a day, daily or weekly) or physiological changes (measured by, for example, self-reported symptoms in a diary or respiratory function tests) and correlated with exposure measurements made at the same time. Each person serves as his or her own control, although a reference panel should be investigated at the same time to adjust for the possible confounding effects of time-dependent factors not related to the exposure (such as weather or reports by the mass media on the incident).

A cohort study is designed for the long-term follow-up of a population selected on the basis of common exposure. The incidence of a particular disease or symptoms of functional impairment is monitored in the population over a long time. The establishment of an exposure register is crucial to setting up a proper cohort study. The control group is often difficult to define. Adequate comparable data on the same population before the event is usually not available. The classification of the study population into groups with different levels of exposure is essential for the analysis. The importance of a good estimate of actual exposure at an individual level cannot be overemphasized. Although some misclassification may be unavoidable, estimates of individual exposure must be sufficiently precise to control and limit biases caused by misclassification.

Case-control (or case-reference) studies, in which cases represent the people with a health condition supposedly related to an incident, are often difficult to perform after chemical incidents. Such a study requires a good case definition (based solely on health status) and this poses a problem if the effects are diffuse and poorly defined. Nevertheless, such studies may be useful for assessing the association of certain health outcomes with the specific characteristics of the incident and the exposure, such as exposure level, time and location or personal activity determining the dose of the chemical. At a later stage, a case-control study can verify the effectiveness of treatment and protective measures, or investigate the factors giving rise to susceptibility. The identification of appropriate control or reference group(s) is crucial to the study’s validity. The selection of subjects for the control group must not depend on exposure status. The only factor
known to differentiate the cases and controls should be the presence and absence of the health condition of interest, respectively.

Table 5 summarizes options for the design of analytical studies and the analysis of the data collected. In each study, an effort should be made to obtain quantitative indicators of exposure for the individuals included. If only qualitative indicators can be obtained, the scope of the analysis is reduced; a gradient of the effects between exposure categories can be demonstrated, but quantitative estimates of the exposure–response relationship are impossible.

**Selection of study groups**

The availability of population data (Box 9) determines the definition of at-risk and control populations. The epidemiologist has to decide whether the health of all members of these populations can be assessed or whether it is more appropriate to study (random) population samples. If the population at risk is small, all members of this group can be evaluated for health and exposure. The examination of all subjects in an exposed community may even be desired by the public and justified on ethical grounds. The expansion of the study group beyond a clearly defined population at risk (through the combination of subjects certainly exposed with people of doubtful exposure status, for example) will dilute the association between the exposure and health outcomes and is not recommended. The control group may consist of a sample taken from the reference population; to ensure sufficient power of the study, the size of this sample may sometimes exceed that of the population at risk.

**Selection of study sample**

The sample size depends on the incidence of the targeted outcome and its relative increase due to exposure (relative risk). Detecting an increase of a rare disease requires a larger sample size than is necessary for a common condition. Similarly, the study of a weaker factor (causing a smaller change in the health of the affected population) needs a larger sample size. Owing to the inherent variability of disease incidence and prevalence, it is advisable to test the consistency of the observed difference in several subgroups of the whole sample (different areas, age groups, sex, etc.). To determine the sample size, published tables and
Box 9. Sources of demographic information useful for the definition of study population and sample frame

**Population register**

*Advantages*
It can provide reliable, up-to-date data on the number and demographic structure of each community, fast and effectively if computerized.

*Disadvantages*
It is expensive to establish and maintain, and there are concerns related to data confidentiality (especially if they are not kept on computer).

**Population census**

*Advantages*
Censuses are conducted every ten years in most European countries. They give relatively precise pictures of the entire population of the country at the specified times. Between the census years, the estimates are adjusted, utilizing data on population movements (births, deaths, migration).

*Disadvantages*
Permanent changes of place of residence are registered in some countries but not in others. Temporal mobility of the population (seasonal or weekly, for example) is very difficult to register.

**Voting lists**

*Advantages*
Voting lists are created on the basis of address registers and (sometimes) updated according to the place of stay during the period of voting.

*Disadvantages*
Voting lists provide a reliable source of information on the part of the population authorized to vote on a community level.
People below a certain age and, often, those with foreign citizenship are excluded. In some communities, those not authorized to vote may constitute a substantial proportion of the permanent residents.
formulas or widely available computer packages, including EpiInfo, can be used (29).

The people selecting the sample for a study should consider that non-availability for a study being conducted rapidly in the period immediately after an incident may be greater than in a normal research situation. This consideration should influence sample size. To assess possible selection bias, the characteristics of the non-respondents should be recorded. It may be necessary to follow at least a part of this group to evaluate the extent to

<table>
<thead>
<tr>
<th>Box 9 (contd)</th>
</tr>
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</table>

### Inventory of housing units, or households

**Advantages**

An inventory provides approximate information on the spatial distribution of the population. The address list may constitute a sampling frame for a population survey following the incident.

**Disadvantage**

The numerical estimates of the population size are not reliable, owing to the possible variations in household size.

### Telephone directories

**Advantage**

Telephone directories offer advantages similar to those of the household inventories.

**Disadvantage**

Their use may lead to a biased identification of the target population in communities or countries where the private telephone is not universal.

### Lists of schools (and students)

**Advantage**

These lists are a reliable source of information on schoolchildren.

**Disadvantage**

Possible discrepancies between the location of the school and students’ place of residence may influence the precision of their classification as the members of the population at risk.
which their non-availability resulted from the exposure and/or health reasons possibly related to the incident.

Selection of a control (or reference) group
When the health effects on an exposed population are analysed, they need to be compared with reference values. These can be based on the data on the same population, recorded before the incident, or from another population (from national statistics or special surveys, for example), assuming that there are no major differences between the two. If this is not the case, ensuring the comparability of populations included in the study requires particular attention.

In environmental epidemiology, the dose–response relationship is of particular importance. Defining nonexposed or control groups is often difficult. Because they usually live in a different place than the exposed population, these groups might differ from it in many ways that are difficult to control for. The establishment of an exposure gradient can make the analysis more relevant and reliable. This can support the notion of a causal association between the incident and the deterioration in health, if the people who have been “more exposed” show a stronger or more frequent reaction. This approach helps to avoid potential biases introduced by using only nonexposed control groups.

In addition, reference values can be collected after the incident through observation of a reference population that is comparable to the exposed one except for the occurrence of the incident. Identical data collection procedures should be planned for both the population at risk and the reference population or, depending on the type of health effect observed after the incident, data from routine reporting of health events should be used. An example of the use of routine data is found in the follow-up study of cancer incidence conducted after the Seveso accident (see Annex) (30).

Special considerations in sample selection for a follow-up study
A specific problem of cohort studies is losses to follow-up. People may leave the area of the incident and that loss may bias the study results, if those more exposed or those experiencing health problems attributed to the exposure are more likely to leave, for example. Mechanisms are required for flagging and tracing the
cohort members. To ensure as complete a follow-up as possible, a means of communication with these people should be established. The exposed group followed does not have to represent the entire population at risk. It can be more effective to include a subgroup with better exposure estimates and greater chances for good participation rates in the follow-up, such as only permanent residents listed in the official register. This method was used in the follow-up of the Seveso accident (21). Other groups that might have been specially exposed but are not resident in the affected area should also be followed. These include rescue workers, fire-fighters, police officers and those involved in clearing the site after the incident.

Sample selection schemes
A survey based on simple random sampling provides the best (unbiased) estimates of the distribution of the exposure and health parameters in the population. Including only (randomly) selected members of the exposed population in the study may raise ethical problems. At the same time, one must avoid conducting the study with volunteers. This may give heavily biased results; for example, only those with visible health impacts may report for the study.

A sampling scheme can be implemented if an appropriate sampling frame is easily available, for example, as a result of special activities at the preparatory stage. A practical scheme, often the most feasible in the post-incident situation, is systematic random sampling: for example selecting every nth patient admitted to the clinic or hospital (according to the admission book). In some situations, sampling frames and methods prepared for another study can be used. Those of a study already under way were used in assessing the health impacts of the Schweizerhalle incident (see Annex). This was also the case in the assessment of the psychological consequences associated with the Amsterdam aircraft disaster, where the existing health interview survey included an appropriate set of questions addressing issues related to the accident (31).

In an emergency, cluster sampling may be more practical than simple random sampling. Data can be collected from all residents of a neighbourhood or from all students of a school with less time and effort than from the same number of subjects living at various addresses or studying at several schools. If the studied characteristics (level of exposure or health status) vary much less
within the cluster than between various clusters, however, the estimates based on the cluster sample may be biased. The risk of such bias decreases if the number of clusters is large: for example, if households constitute the clusters and these units are randomly selected from the address register covering the whole population.

If subgroups of the population at risk can be defined with different characteristics possibly related to the exposure or to the health reaction to the incident, a stratified sampling scheme is advisable. The sampling frame must be available for each of the strata. If the study addresses the exposure or health effect estimates for each of the strata, not just the population as a whole, a sufficiently large sample is needed from each stratum; this means an increase in the size of the total sample.

**Data analysis and interpretation of results**

As in all epidemiological studies, competent, careful and critical analysis of the data and its interpretation is a central requirement of studies following environmental incidents. All possible alternative explanations should be taken into account. A description of the requirements for data processing and analysis can be found in numerous publications (28). After the data are collected, epidemiologists with basic training in statistical methods should quickly make an initial analysis, using EpiInfo (13) or other simple computer packages for data processing and analysis. More advanced interpretation may require the participation of experienced biostatisticians.

**Box 10. Health assessment – summary**

- The use of existing, routinely collected data should always be considered the method of choice in assessing the health consequences of an incident.
- If necessary, special data collection should be designed, strictly following the requirements of design methodology for epidemiological studies.
- Exposure information is needed to assess the link between health and exposure due to the incident. It may be necessary to include elements of exposure assessment in the health study.
- The timely analysis of data and its critical interpretation are central to the epidemiologist’s activity following the incident.
The study results, including negative results, must be reported to a wide scientific community in order for them to be accessible to those who have to deal with similar problems. Each step of the investigative process – including decisions to omit data, participants or potential sources of variation – has to be documented accurately. The method of analysis, including the statistical model with its underlying assumptions, should be stated. The results should be presented as an association – if possible, as a dose–response relationship – with discussion of all potential biases that could reasonably be expected to affect the validity of the results.
Supportive action

Cooperation
As stated, the epidemiologist’s goal, as a member of a multi-disciplinary emergency response team, is:

- to prevent or minimize the adverse health consequences associated with an incident;
- to optimize the decision-making process in the management of the response; and
- to minimize the risk of such incidents in the future.

The response will be adequate and appropriate only when all those participating in incident management accept that they are members of a team and that their roles and responsibilities within it will alter with the nature of the incident and the phase of the response. During an incident, epidemiologists are members of the public health team handling the implications of the event for human health. This is only one group within the total structure of response management. The managers of the emergency response team should appreciate the contribution that epidemiology can make, particularly in establishing priorities for action, and proper decision-making based on timely and appropriate information.

Once the epidemiological team has been designated, certain key requirements need to be met. The team leader must rapidly identify those with whom the group has to cooperate to fulfil its allocated tasks and the person within the management structure to whom it should report, as well as the frequency of such reports.

The emergency services may ask the public health team urgently to address several types of question:
• the toxicological nature of the released substances (or combustion products in a fire) and the likely health effects;
• advice on clinical management, such as the prediction of health effects as a basis for patient monitoring;
• the types of casualty to be expected;
• the risk of health effects to emergency personnel;
• the risk of environmental contamination and its possible effects on human health;
• the potential effect on public health of the emission, including the identification of sensitive populations; and
• in a continuing incident such as a chemical fire, advice to emergency officials on the health criteria for evacuating sectors of a community.

The public health team should have access to external expertise in clinical toxicology, occupational hygiene, environmental chemistry and occupational medicine, as well as epidemiology. The team may have either a local or a national base, but it is important that the members have met before the incident (during the preparatory phase) and are able both to come to the scene of the event, if necessary, to provide direct advice, and to arrange for environmental sampling and health data collection. The team should include health scientists and practitioners from the chemical industry, who may have considerable expertise and resources in dealing with major incidents. The epidemiologists have a key role in ensuring the quality of the data collected by the team.

The team needs expertise in hazard identification, exposure estimation, dose–response assessment and risk characterization. The team’s work includes identifying the community’s health needs and responding to them. Examples include attending to the psychological effects of chemical disasters, with the public health team playing a leading role in ensuring that the appropriate preventive health response is made.

The active participation of representatives of industry – from either the enterprise directly associated with the event or other companies or expert organizations – facilitates the management of an incident. These bodies may have a range of experts with unique skills and immediate access to information essential to appropriate health risk assessment. Their role within the team
must be clearly defined, however, and potential conflict between their professional contributions and their organizational responsibilities must be recognized.

Public opinion tends to assume that industry’s legal defaults and/or products are responsible for an incident. The correctness of this assumption is usually determined later, after rigorous investigations. Epidemiologists should be cautious in their evaluations; in not doing so, they would not only fail to adhere to a scientific behavioural code but might also impair the collaboration needed to identify precise causal associations (and sometimes legal responsibilities). It is essential, for example, that the public health sector manage the studies, and not delegate the task to industry.

Epidemiologists work in support of public health agencies. Whether epidemiologists are employed in the public or health sectors, academic or national institutes or industry, their knowledge, skills and data should be available to all of these in the response to an incident. To fulfil this role, the epidemiologist needs to take advantage of the skills and knowledge of the colleagues who will help to amass and analyse relevant data and thus to determine the response needed. These tasks require the cooperation of a range of different professionals, including primary care workers, specialists in referral centres, local environmental health officers or hygienists, and staff and specialists in laboratories and toxicology centres. As well as participating in the design, implementation and analysis of the epidemiological studies, all contributing professionals need to feel ownership of them, agree the findings and take part in their dissemination.

In many countries, poison information centres provide information needed for health-related responses to major chemical incidents. These centres possess relevant data on the diagnosis, treatment and rehabilitation of people affected in an emergency, as well as on the features of prolonged exposure and potential long-term effects. They provide ready (ideally, round-the-clock) access to advice on acute and chronic poisoning by chemical, biological and/or radioactive agents. The annually updated listing of the poison centres registered by WHO is included in the INTOX computer database of the International Programme on Chemical Safety (IPCS).
Public authorities at the regional and national levels have the major responsibility for protecting the health of the population. They therefore take the lead in developing health-related components or preparedness plans as part of overall emergency planning. Each country needs to have the means to organize the collection, collation and dissemination of information for use during both the planning for and the response to an environmental incident. This information is essential for improving decision-making and minimizing the adverse public health consequences of incidents. Appropriate epidemiological, laboratory and toxicological skills are required for the rapid evaluation and assessment of risks. Such capacities may not be available locally and a team of experts with the appropriate expertise, including expertise in environmental monitoring, needs to be available for rapid deployment, especially in large or unusual incidents. Such groups need regional, national or even international planning and development. Public health officials at the local level should be aware of the skills of such teams, their location and the means of rapidly calling for their assistance at any time.

**Dissemination of Information**

In incident management, the importance of keeping the public informed tends to be underestimated. Coordinated public relations should be part of the management of the event itself and are important for political reasons. Confused and controversial messages have a negative influence on both the public and the personnel dealing with the incident, and may cause panic. An information strategy with certain rules and procedures should be implemented as soon as an incident happens. It should be based on a plan, and the people implementing the strategy should already be acquainted and have established good working relationships. In such a situation, the vehicles and channels to be used should already have been defined and the roles of the different collaborators in the event recognized.

In the acute phase, the most important task is adequately to explain the results and limitations of the risk assessment performed by the people managing the event. The areas to be covered include hazard, dose–response estimation, exposure assessment and risk characterization. This risk assessment has to
be communicated in a way that enables the target audience to understand and interpret the information supplied. Clinicians working in both primary care and hospitals must be informed of this appraisal. A correct understanding of the risk levels reduces the anxiety caused by overestimating the risk and helps to reduce the significant exposure caused by underestimating the risk.

As well as receiving information on risk assessments, other public health professionals and those involved in direct patient care should know how they can contribute to the epidemiological assessments that are under way. Effective communication should be maintained with everyone involved in incident response. They will need technical information and advice on specific epidemiological aspects of the management of the incident, and information on the outcome of surveillance and other activities. Response personnel should be briefed on the role of epidemiology in the response and how they can contribute to the epidemiologist’s work. Specific health data will be required, and these can be gathered by the emergency and post-emergency health teams. It should be remembered that, in the midst of an incident, responding staff may not receive adequate updates on the crisis as a whole, and may have less opportunity to receive information from the mass media than the exposed population. Such staff may also be residents of the affected area and need briefing on both personal and community risks.

Effective communication can be accomplished through public meetings or groups of key individuals. Public meetings, at which epidemiologists present information and answer questions from the exposed population, are the ideal, but these may not be feasible in view of geographical conditions or the characteristics or knowledge of the potential audience. As an alternative to public meetings, results can be reported to local opinion-formers or elected representatives, assuming they have the population’s confidence. Media statements and subsequent interviews can be used to reach as large an audience as possible.

Ideally, the lines of communication and an ethos of mutual trust will have been established before the incident. This requires the acceptance and involvement of the public, the press and co-workers in incident management as legitimate partners. In
addition, communications should be carefully planned, and evaluated for effectiveness. The people managing the incident must:

- listen to the concerns expressed;
- be willing to be honest, open and frank;
- have an understanding of the role of and constraints on the media; and
- have the ability to avoid jargon and show understanding and empathy.

The effect of the communications strategy should be continuously evaluated throughout the incident; if needed, the strategy should be modified.

The maintenance of an atmosphere of cooperation, particularly with the local community, is essential. To retain public confidence in the impartiality of the study team, the affected population should be the first recipients of the results of this work. Ideally, the information will be correct and unambiguous. This may be difficult where available data are limited and different interpretations are possible. People expect certainties and definite answers from both officials and scientific studies. Unfortunately, uncertainty is not a fixed quantity or always reduced by scientific research.

Critical situations result when the groups potentially affected do not trust the people managing the response or those advising them. Messages to the public must use simple language that is intelligible to people without a technical or scientific background. In particular, the public needs to understand and accept that epidemiological studies examine populations rather than individuals, and that their results reflect this. For example, although an incident may affect the health of a small number of people, the epidemiological evidence might be not strong enough to show a statistically significant effect in the entire exposed population.

To ensure that the public understands the information provided, its presentation may need to be repeated or changed over a period of days or weeks. Widely distributed, clearly written information bulletins may be useful. The people exposed and their relatives should have the chance to ask questions about the potential dangers and to discuss their individual risks of present or future health effects with experts. Further, those managing the
SUPPORTIVE ACTION

public information response must identify and address any misconceptions within the community. This process is complicated when information about the hazards is limited, if not nonexistent.

Problems of communication between epidemiologists and the public may arise at different points: the first-hour prediction of risk (including the choice of mathematical models and size of statistical errors considered to be acceptable), interpretation of early clinical events, evaluation of the need for ad hoc epidemiological studies, and assessment of potential bias in the results. Ethical guidelines for risk communication have not been defined, but measures for converting an “arrogation of wisdom” into a “stewardship of wisdom” were suggested to scientists about 20 years ago (32). A whole range of situations lies between two extremes: circumstances in which the prediction of risk is reliable and the implementation of preventive measures is feasible, and cases in which the measurement of risk is uncertain, there are no alternatives to continued exposure and there is no treatment for the relevant condition (33–35).

Those who study the health consequences of an incident must disseminate the results to fellow professionals. This is both to alert them to the identified health effects on the exposed population and to reassure them where effects are absent. The results should be communicated directly, either in writing or orally, as agreed with the local public health officials. Making the information available to the whole scientific community is equally important. Such studies may produce invaluable knowledge for people confronting a similar event. Ideally, studies will be exposed to peer review and published in readily accessible journals. Peer review may help to ensure that an epidemiological study is well designed and properly conducted, and may complement the epidemiologist’s inferential process. Further, in the eyes of the public and political authorities, peer review may provide credible support for a decision not to carry out a study, which is likely to be unpopular.

Researchers should always insist on the publication and unlimited dissemination of the results. It is unethical to perform such work and not to make the findings available to colleagues, to enable them to make risk assessments and respond appropriately when confronted with similar public health emergencies. Negative as well as positive findings are invaluable. To reduce the problems of publication bias, papers should be lodged with the
clearing-house that is being established within the WHO collaborating centre at the Cardiff Institute of Higher Education in the United Kingdom (see Box 11). This will permit the results of such investigations to be collated and thus made easily available.

Box 11. Terms of reference of an international clearing house for major chemical incidents at a WHO collaborating centre

The terms of reference are:

- to investigate the possibilities of international collaboration and cooperation;
- to investigate methodologies for the establishment of national surveillance programmes for major chemical incidents;
- to develop guidance materials and standardized documentation for the reporting of major chemical incidents, including what to report, to whom and by what mechanisms;
- to collate and analyse the data received on such incidents and prepare reports in a form that will be useful to countries in planning their response to such incidents in the future;
- to disseminate such information to the regional offices of WHO for onward transmission to WHO Member States;
- to make such information available to other WHO collaborating centres;
- to develop an international database on the problems encountered in dealing with major chemical incidents;
- in collaboration with WHO regional offices and other collaborating centres, to develop training materials and methods, to hold training courses, workshops and seminars, and to participate in personnel development programmes for the management of major chemical incidents; and
- to develop a multidisciplinary team that can be deployed to provide advice on both dealing with a major chemical incident and conducting short-, medium- and long-term follow-up.

The WHO collaborating centre for an international clearing-house for major chemical incidents is the University of Wales Institute, Western Avenue, Cardiff CF5 2YB, United Kingdom (telephone: +44 1222 506852; fax: +44 1222 506983; e-mail: gcoleman@uwic.ac.uk).
Further, the results of epidemiological studies should be circulated to policy- and decision-makers and regulators at the local and national levels. The scientific and health information gained from the incident and any lessons learned about management may need to be incorporated into local incident management plans. They may also highlight the need for changes in the regulatory or legislative framework to prevent the occurrence of future events that may affect public health.

Information is the critical element in all phases of the response to a public health incident. In the planning phase, information and communication needs should be established and the means of obtaining and disseminating information should be determined. The people involved in managing the incident, the health care professionals and the public have different needs. For effective dissemination of information once an incident has commenced, identified chains of communication are essential. These must be established in advance among all appropriate groups; the people tackling this task should remember both the range of potential events and that normal means of communication may not be functioning during an incident.

The simplest approach in selecting the method of communication is to be open, to be honest and to avoid gimmicks. Ideally one spokesperson should speak on behalf of the team managing an incident, or at least the team should issue public statements based on consensus. Team members should speak solely on their areas of expertise and then only within the context of the agreed position. There is always the risk that spontaneous remarks may cause distress to the exposed population and difficulty for the people managing the incident. Possible communication opportunities and constraints should be identified, such as the scheduled time of news broadcasts, newspaper deadlines, etc. To do this requires the definition of communities that may be affected and the creation of an inventory of existing contacts during the planning phase. The appropriate local contacts – community leaders and opinion formers, public health officials and health care professionals – should be documented. Draft information sheets should be prepared for the public and professionals. Before any information is disseminated, the target audience must be defined. Experts like to use statistics, but other people may have a fundamental distrust of them and base their
perceptions of risk on a wide range of values, philosophies, concepts and calculations.

Decision-makers and scientists often become frustrated with the mass media. They expect journalists to report risk information accurately and assign the media some of the blame for public confusion. Journalists are trained to report events that relate to well known topics of current interest and that can easily be described in visual terms. Stories that do not fit these criteria are rarely used. Nevertheless, the media are an important source of hazard and risk information for many people and will play a crucial role in providing balanced perspectives. Researchers should spend time with media representatives to explain the main findings of their research and the main messages to convey to the people.

Training

It is impossible for public health authorities to be completely prepared for environmental incidents. Much of what can be done after an incident depends on the rapid, systematic collection of both routine and non-routine data under difficult conditions. Factors affecting the ability to collect such information include the training, expertise and ability of personnel such as environmental epidemiologists. Teaching still centres on major incidents or disasters with multiple casualties, and the use of immediate death and injuries to judge the severity of the events. There is not enough emphasis on smaller incidents that, owing to their frequency, may have important effects on public health.

Public health practitioners need to be trained to deal with chemical emergencies in the community and to take a leading role in coordinating the response of the health sector. It is essential that this role be planned and well organized in advance of any emergency. To achieve this, public health practitioners need to collaborate with emergency planners and hospitals to ensure that the emergency response automatically includes the public health sector with its predefined role. Further details on the role of the public health sector in preparing for and responding to major chemical incidents are given in a document by WHO, IPCS, the Organisation for Economic Co-operation and Development and the United Nations Environment Programme (36).
The training of epidemiologists should include issues related to the unique aspects of an acute incident, including exposure assessment and risk characterization. Training is needed in both the appreciation of the potential contribution of epidemiology to the management of an incident and in the skills needed by medical practitioners and epidemiologists to make this contribution. An epidemiological perspective is useful to the wide range of professionals concerned with the adverse health effects provoked or exacerbated by environmental factors. The organizational skills of communicable disease epidemiology are useful in the response phase, and the skills of chronic disease epidemiology are essential in examining long-term effects.

Decision-makers need timely and appropriate information. They must appreciate that epidemiologists play a vital role in developing reliable information on the health consequences of an incident, conducting surveys and investigations where necessary, providing advice on health problems that may arise and establishing priorities for action. Decision-makers need to understand the contribution that epidemiology and epidemiologists can make to the successful management of an incident or disaster; this demands an appreciation of epidemiological methods. While some theoretical knowledge is required, an exposure to practical epidemiology is essential. Decision-makers can best acquire these from case studies of incidents and from simulation exercises. The leaders of various professional groups that may be involved in the different phases of an incident need a similar appreciation of epidemiology.

A cadre of epidemiologists with knowledge of and skills in environmental epidemiology is essential. Depending on the local public health system, it may comprise public health officers with additional training or regional, national or international experts able to respond rapidly to incidents. Such people must be trained in the public health management of incidents, risk assessment and environmental epidemiological methods, including devising a plan for a descriptive epidemiological study of an environmental health problem and a basic analysis of the data. Such epidemiologists are able to understand and apply to environmental health the basic principles of epidemiology. In particular, they are able:
• to understand:
  – the adverse health effects of common chemical, physical and biological risk factors;
  – the concept of exposure routes and issues related to measuring environmental exposures;
  – issues related to epidemiological study design;
  – issues related to exposure and health effects surveillance;
  – the roles of and the need to cooperate with other professionals when studying or managing environmental health problems;
  – the principles of risk, risk assessment and risk communication;

• to plan and implement a descriptive epidemiological study;
• to perform a basic analysis of data; and
• to suggest areas for health care development based on the assessed health needs of an affected population.

Full-scale, complex, ad hoc environmental epidemiological studies are collaborative endeavours involving epidemiologists, statisticians and other specialists. Skills systematically developed through studying common environmental exposures and their health effects are essential for the assessment of the health effects of environmental incidents.
References


69


Annex: summaries of selected incidents

The Environmental Accident at Schweizerhalle

Background

On Saturday, 1 November 1986, the storehouse of a chemical factory in Schweizerhalle, Switzerland, containing 1300 tonnes of chemical substances (mainly agrochemicals) burned down. Schweizerhalle is located about 5 km from Basle, a city with about 200,000 inhabitants. The fire was discovered at 0.30 a.m. It was described as extremely hot, and probably either caused complete combustion of products or brought the combustion products to a height at which a strong wind carried them to the Black Forest. At 3.00 a.m. the fire brigade decided to use water to extinguish the fire, making the combustion process incomplete. A foul-smelling cloud developed, and was driven by the ground winds to Basle. The stench lasted several days and frightened people in Basle more than the toxic flows into the Rhine, which caused international consequences (1).

Only on 6 November did the complete list of stored products become known; it contained:

<table>
<thead>
<tr>
<th>Products</th>
<th>Amounts (tonnes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acid phosphate esters</td>
<td>859</td>
</tr>
<tr>
<td>Chlorinated organic compounds</td>
<td>16</td>
</tr>
<tr>
<td>Organic mercury compounds</td>
<td>11</td>
</tr>
<tr>
<td>Other agrochemicals</td>
<td>100</td>
</tr>
<tr>
<td>Adjuvants, colorants, solvents, stabilizers</td>
<td>364</td>
</tr>
<tr>
<td>and raw materials</td>
<td></td>
</tr>
</tbody>
</table>

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1 This section is based on the work of Ackerman-Liebrich et al. (1), Braun-Fahländer et al. (2), Heierli (3) and Hellenstein et al. (4).
Investigations
The following investigations were proposed to describe the impact the fire might have had on the health of the local population:

- an analysis of daily mortality;
- an analysis of inpatient and outpatient attendance at the hospitals in the region;
- an analysis of patients treated in private practice;
- a survey of symptoms in different population groups;
- surveillance of fire-fighters involved in fighting of the fire; and
- long-term surveillance of congenital malformation (register).

Short-term effects
An analysis was made of daily mortality in the region over a six-year period (1980–1986). Mortality did not increase on 1 November or on the days immediately following. A peak of 21 deaths (instead of the 12 expected) occurred on 8 November, a week after the fire. There is no plausible hypothesis connecting the observed peak with the event.

All hospitals in the region were asked to provide the number of admissions to medical wards and the daily outpatient attendance during October and November. These figures revealed no difference in attendance. The medical association sent a questionnaire to its members, which revealed that 1363 people had consulted physicians because of symptoms related to the fire. It could not be judged from the questionnaires whether the patients or the physicians attributed the symptoms to the fire.

On 1 November, a population-based study of respiratory symptoms of preschool children (recorded on daily diary forms by their parents) was already in progress. It could be used as an indicator of the health effects of air pollution levels experienced in Switzerland. Details on the methodology of this study have been reported elsewhere (2). On average, 30% of the children experienced one or more symptoms on a particular day. On 1 November, symptom prevalence increased to 50% in Basle; no increase was observed in Zurich. Further, the symptoms seemed to have persisted until the end of the study period and a high proportion of children experienced three or more symptoms.
The data were analysed by several statistical methods. It was assumed in the statistical experiments that the time of the accident was unknown. Two different methods used for this purpose found 1 November to be the most likely time of an accident. In addition, the proportion of symptoms reported was significantly higher than forecast (4).

Because the sample participating in the study of children at the time of the accident was rather small and a strong effect was not anticipated at the time, it was decided to send a questionnaire to all former participants and their families. This was the most quickly available population sample. The 516 Basle families that had participated during the year were contacted; 423 sent back 1589 questionnaires. The questionnaire asked whether the respondents thought they had experienced symptoms related to the fire on 1 November. Symptoms were then detailed by organ system (respiratory, gastrointestinal, skin, etc.) and date. Because the sample described was composed mainly of young children and their parents, a further sample of adults was drawn from the population registry in Basle (300) and the suburbs (300). The people from this sample were invited to an examination. An interview concerning symptoms experienced in connection with the fire of 1 November was conducted and hair, urine and blood samples were collected.

Respiratory symptoms were more frequently recorded in the group with young children. Mothers of young children frequently mentioned nausea, vomiting or diarrhoea. But eye symptoms and headache were also more prevalent among the parents of young children. Those who smelled the smoke experienced more symptoms than those who did not. This might be an indirect measure of exposure. From the adult sample, five people had experienced symptoms of a degree that necessitated medical attention. Extrapolation to a city with a population of about 200 000 estimates that between 1400 and 3600 people would have sought medical attention, which is more than the 1363 who had consulted in the report of the medical association.

In a laboratory test in the general population, hair and urine from a random sample of the population were analysed for mercury. No elevated mercury levels could be found.

As to the health of fire-fighters, the blood of those who fought the fire was examined. A total of 428 men were examined between
6 November and 14 December 1986. The symptom questionnaire applied in the other studies was not used in this investigation. The 93 men who entered the enterprise services after the event served as controls (3). One fire-fighter had to be taken to hospital with a fit of hitherto unknown epilepsy. A significant increase could be found in free iron and of gamma-glutamyl transpeptidase. When the fire-fighters were subdivided into those who actually fought the fire and those who later worked on the fire site, it could be shown that this increase in free iron was present only in the first group. A similar finding was reported (5) in workers exposed to organic sulfides in a pulp plant. These results cannot be interpreted further, since no attempt was made to examine the workers clinically or to ask them about symptoms. The re-examination of those with elevated plasma levels, performed by the occupational health service of the enterprise in February 1987, revealed only normal values (3).

Long-term effects
Discussion on the possible long-term effects of a one-time exposure to unknown concentrations of unknown or partially known substances tends to be emotional. Long-term effects of the Schweizerhalle incident could include cancer, poor reproductive health or morbidity in general.

Cancer can probably be excluded in this case because a single exposure is unlikely to lead to cancer without causing previous serious health effects. In addition, phosphoresters are not among the pesticides discussed for carcinogenicity (6). Effects on reproductive health could be measured in terms of increased rates of abortion or congenital malformation. The EUROCAT system (7) was introduced in Basle on 15 May 1987, but data were incomplete in the beginning: the system requires a certain time to become reliable. As to morbidity, the expert committee appointed by the Federal Government of Switzerland commented on a preliminary report. Its recommendations included continuing the study on air pollution and health for another year as a comparative study of Basle and Zurich, in order to exclude an increased prevalence of respiratory symptoms in Basle due to a weakening of the respiratory system. No difference in the prevalence of symptoms was found between the two cities in the study, and an increase in average symptoms observed per child and day was found in both cities.
Discussion
The health effects of the Schweizerhalle fire can be described as a general increase in respiratory symptoms in the population, which in about 1% necessitated a visit to a physician. The effect seemed more pronounced in preschool children and in people suffering from chronic diseases, especially asthma. No serious or persistent health damage was reported in the fire-fighters who were supposed to have been exposed, except for one man who was admitted to hospital with an epileptic fit. The examinations were voluntary and conducted by the firm’s own health service. Most took place one month after the event.

The most reliable sample examined here seems to be the parents of preschool children in Basle who were keeping diaries for respiratory symptoms in their children during the event. The prevalence of symptoms in this group was higher than before and higher than in Zurich. It was also higher than in people contacted within the first week of the fire and the group from the general population interviewed one month later. The pattern of symptoms (respiratory, followed by gastrointestinal symptoms (such as nausea and diarrhoea) and irritated eyes and skin manifestations) was very similar in the different population groups, with the exception of headache. The psychological strain on the population was considerable. Fear and distrust of official statements prevailed. This might have led to an increase in symptoms, either felt or reported.

Conclusion
Two basic issues are involved. The first is the importance of familiarity with the potential health hazards in one’s surroundings and the reduction of these hazards whenever possible. Before the Schweizerhalle incident, the issue of disclosing storage and production processes and the substances stored and produced was discussed only in general terms. After the fire, however, the attitudes of the government, public and industry changed completely. As a result of the Schweizerhalle fire, an agency for the control of chemical safety was established in Basle. Its task is to register all stored products according to the risks involved and to control the implementation of safety regulations. Further, a new ordinance dealing with countrywide accidents and hazards was implemented, forcing industry to disclose production and storage data on hazardous substances and to detail emergency plans.
The second issue highlighted by the incident is the need to prepare epidemiological expertise and analysis for use once an event occurs.

The Seveso Accident

Background

A chemical incident occurred on 10 July 1976 near the industrial town of Seveso, northern Italy, in a small chemical plant, shortly after closing down for the weekend. It was concluded that a runaway reaction in a vessel for the synthesis of trichlorophenol caused an uncontrolled surge of the temperature and pressure. The safety valve of the reactor ruptured and a fluid mixture of chemicals burst into the air causing contamination of the surrounding populated area.

Early and unequivocal signs of contamination appeared in vegetation, in domesticated and wild animals and in people. In particular, skin changes were noticed in children living close to the plant. When, on the tenth day, 2,3,7,8-tetrachlorodibenzop-dioxin (TCDD) was publicly recognized as the main component of the toxic cloud, fear arose for the health of human beings.

Apart from the health effects, the incident was an obvious social and economic disaster, and people living in the incident area suffered from anxiety, insecurity, mental stress and isolation for months, if not years. Those in the most contaminated area had to leave their homes. More than 50 handicraft and industrial firms were forced to evacuate, abandoning buildings, goods, machinery and products. Many of the buildings were razed.

Investigations and results

In this emergency, health-related post-disaster activities had three main tasks:

- defining the exposure, identifying its nature, characteristics and extent and identifying the number of people involved;
- carrying out preventive measures and managing the identified risks; and
- establishing short- and long-term health surveillance programmes.

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This section is based on the work of Bertazzi & di Domenico (8), Bertazzi et al. (9,10), Mocarelli et al. (11), Pesatori (12) and Pocchiari et al. (13).
An extensive programme monitored different environmental systems and media (soil, vegetation, water, animals, etc.); this allowed the determination of the level of exposure and the extent of contamination, and the behaviour and fate of the TCDD released into the environment. Environmental analyses in the area provided the basis for delineating zones with different levels of contamination. At various parts of zone A, the most heavily contaminated, the average soil levels of TCDD ranged between 16 mg/m² and 580 mg/m². Using the official residence registers at the vital statistics offices of the towns within the incident area, subjects were assigned to one of the three exposure zones (A, with some 700 subjects; B, more than 5000; or R, with over 30 000) or to a surrounding non-contaminated territory (around 220 000 subjects). In addition, information about exposure was derived from signs and symptoms, such as skin burns and eye irritation, that affected people after the incident. Thousands of blood samples were collected. Each sample was stored and later used for measuring serum TCDD levels and for blood chemistry testing.

The regional government set up a special office for Seveso to manage all post-disaster programmes, including the rehabilitation of the area. One of the office’s four branches was concerned with epidemiological and health activities.

The complex crisis affected the ability to plan and conduct valid epidemiological investigations. This complicated the task of evaluating the early and mid-term effects following the incident. Several different teams were called on the scene, and cooperation among them and coordination of activities were often difficult.

The most relevant finding of the assessment conducted at an early stage was the identification of nearly 200 cases of chloracne after the screening of thousands of children. Investigations on congenital malformation and cytogenetic findings failed to demonstrate any obvious effect related to TCDD exposure. Liver enzymes showed a temporary increase in children living in the most polluted area. Major problems in interpreting the results of these studies arose from, for example, the often insufficient size of the samples, the lack of proper control groups, the scarcity and/or uncertain validity of existing records, and the incomplete standardization of ascertainment and measurement methods and procedures.
Investigations of long-term effects (mortality and cancer incidence) were designed later. Experience in conducting occupational follow-up studies notably facilitated their planning and conduct. The study population comprised all subjects ever residing in one of the 11 relevant towns (4 with TCDD contamination and 7 serving as controls) at the time of the incident and throughout the following 8 years, to take account of the persisting environmental contamination. It also included the people who left the area after the incident and the newborn. The tracing of study participants and ascertainment of their vital status had a success rate of more than 99%. Causes of death were ascertained through the municipal vital statistics offices throughout Italy. For cancer incidence, the study relied on the hospital admission registration system of the Lombardy region, where the study area is located (the emigration rate outside the region is 0.6% per year). For a ten-year study, the number of individual medical files identified was 41,801, of which 41,778 were successfully reviewed. An ad hoc investigation estimated the proportion of true cases not detectable because of erroneous records; for malignancies this proportion ranged from 2.6% to 6.8%.

The ten-year mortality study revealed an increased occurrence of cardiovascular diseases that might be related to stressors caused by the disaster. The cancer incidence study revealed an increased risk of hepatobiliary cancer in subjects living in zone B, especially in those living in the area for more than five years. In the same area, men exhibited an increase in leukaemia, and women experienced an increased incidence of multiple myeloma and myeloid leukaemia. Subjects living in zone R, the most populated though least polluted area, had an elevated incidence of soft-tissue sarcomas. A possibly reduced incidence of hormone-dependent tumours, such as breast and endometrial cancer, was suggested in the most polluted areas (zones A and B). All these findings are consistent with the previous knowledge of the effects of TCDD on animals and human beings.

Discussion and conclusion
The follow-up of mortality and cancer incidence was planned to continue for at least 20 years after the incident. Knowledge of the mode of action of TCDD, including at the molecular level, has advanced significantly over the past few years. Case-control studies
are investigating the possible role for some recently identified markers of susceptibility to TCDD in selected samples of the population (people with chloracne, TCDD-associated cancer, etc.). These late studies have been made possible by the close collaboration of scientists from different fields and public health researchers. The experience gained underlined the need for the early involvement of epidemiologists in planning, intervention and research.

The Shetland Oil Spill

Background

On 5 January 1993, the tanker *Braer* ran aground on the southwestern coast of Shetland, United Kingdom. Over the following 6 days, it leaked 85 000 tonnes of crude oil, the maximum discharge occurring as the ship broke up on 11 January. Concerns were expressed about the immediate and long-term health effects on the exposed population, and the statements of certain individuals and organizations exacerbated public anxiety. There were anecdotal reports of acute toxic symptoms, mainly of a short-lived, exposure-related nature. The volatility of the oil and the extreme weather conditions resulted in its being blown over land, exposing soil, crops, buildings, animals and human beings to hydrocarbons as vapour, droplets and oil/water emulsions. Dispersants were sprayed from the air, falling over land as well as sea. Some of the constituents of the oil were known to have potentially carcinogenic effects.

Epidemiological investigations of major oil spills have been infrequent, have focused mainly on workers involved in clean-up operations rather than residentially exposed people, and have been performed at later stages in the incidents. Similarly, studies on hydrocarbon hazards have concentrated on occupational rather than residential exposure and have emphasized chronic rather than acute symptoms. A study was designed to determine the human health effects of the oil spill on the Shetland population. It did not offer a health check, which is a clinical matter between a person and his or her general medical or occupational health practitioner. The Shetland Health Board’s Research Ethics Committee approved the study. It began within a week of the start of the incident.

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3 This section is based on the work of Campbell (14), Campbell et al. (15,16) and Foster et al. (17).
Investigation
The method utilized was a cohort study with comparison against controls, with exposure status being assigned on the basis of residence. The exposed group was defined as the people permanently resident within a 4.8-km radius of the wreck and present in that area at any time after the incident, a decision based on the geographical area most affected and a practical study size. An unaffected location, 96 km north of the incident, was used as a control area. A statistical power calculation was performed to determine the numbers of exposed and control participants required. Controls, matched for sex and age distribution, were randomly selected and those who confirmed no contact with the study area from the onset of the incident were invited to participate.

Information was collected using a personally administered structured questionnaire. It covered personal details, past medical history, current drug treatment, perception of health, and the presence or absence and date of onset of specific symptoms occurring both during the two weeks preceding the wreck and during the time between the wreck and the interview. No definitions of symptoms were given or clinical examinations performed. Participants were asked to state whether their activities since the incident had principally taken place inside or outside a building as a proxy for exposure dose. Owing to the non-uniform geographical distribution of participants, it was not possible to allocate degrees of exposure based on their place of residence. A telephone survey of non-participants within the exposed population was performed utilizing a one-in-four systematic sample with substitution. Resource constraints precluded any follow-up of control non-participants. Height and weight were measured and respiratory function estimated by peak expiratory flow. Urine analyses were performed and laboratory testing carried out for hydrocarbon toxicological markers. Haematological estimations were determined, biochemical tests were performed for liver and renal function, and toxicological tests were made for hydrocarbons. All results were reported to the participants’ general medical practitioners, from whom they were available to participants.

In June 1993, the participants were invited to take part in further studies. The original questionnaire was extended, encompassing the participants’ perception of their health since the incident, changes in reported health and the attributed reasons, and
long-term symptoms potentially associated with exposure to oil and hydrocarbons. A systematic sample of non-participating exposed people was surveyed by telephone to ascertain their reported health experiences. To study psychological effects, participants aged 16 years or over self-completed a version of the general health questionnaire with 28 questions. Repeat measurements of biological markers were performed.

The long-term follow-up of the exposed cohort continues by means of the “flagging” of national cancer and mortality registers.

Results
The principal health effects arose on the first and second days of the incident and included headache, throat irritation and itchy eyes. No significant differences between the exposed and controls were found for any of the biological markers. Toxicological studies did not demonstrate any exposures known to affect human health. In the follow-up phase, the physical symptoms identified after the event had passed. Significantly more exposed individuals considered their health to have deteriorated since the incident, although less than half attributed this to the event. No differences in biological markers were found. The exposed people showed more anxiety and somatic symptoms than the controls.

The results of the two phases of the study were reported to the sponsoring body, presented to the exposed population at public meetings and published in peer-reviewed journals. The opinions of members of the public on the activity were sought.

Conclusions
1. In Scotland, epidemiologists work in support of the public health managers of an incident. In this case, a team from the Environmental Health (Scotland) Unit (now the Scottish Centre for Infection and Environmental Health) performed the study on behalf of the Director of Public Health, Shetland Health Board.

2. The people of Shetland were consulted about their views on carrying out such a study and its possible methods. The results of such studies must be communicated in an acceptable manner to those potentially exposed. Lessons were learned from the Shetland study.
3. Speed is of the essence but should not be secured at the expense of scientific rigour; this study began within six days of the start of the incident.

4. Such studies are cooperative activities involving several disciplines at not only the local but also the national and possibly the international level. Many people will come forward with their own proposals for studies after an incident.

5. Incidents such as the grounding of the tanker are rare and therefore unique training experiences; four trainee epidemiologists participated in the work.

6. Negative findings are as valuable as positive ones.

7. Groups with occupational exposure during an incident should be studied, as well as those with residential exposure.

**Toxic Oil Syndrome in Spain**

**Background**

The first evidence of this incident (early May 1981) came from a number of children admitted to hospital with an unusual association of fever, pleuroneumonia, rash, myalgia and eosinophilia. Within a few weeks, some 20,000 people were affected in Madrid and in the north-western provinces of Spain; more than 300 died (18). This episode is unique for at least two reasons: the novelty and the etiology of the disease.

First, medical nosology had no previous record of toxic oil syndrome. Although currently interpreted as a non-necrotizing vasculitis affecting several organs, its pathogenesis, long-term sequelae and possible late complications are not yet understood.

Second, although a causal association has been established with a definite source of an exogenous agent, the agent itself (most likely a chemical) remains unknown. The source was allegedly edible olive oil contained in typically shaped, unlabelled, five-litre plastic bottles, sold by travelling salespeople in April and May of 1981. In fact, a sizeable proportion of this oil (hereafter

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4 This section is based on the work of WHO (18), Abaitua Borda et al. (19) and Kilbourne et al. (20).
called illegal oil) was rapeseed oil, imported for industrial use after denaturation with aniline (as required by Spanish law). It had later been illegally processed to look like olive oil, although substantial amounts of aniline derivatives were subsequently detected by chemical analysis. Assembling the evidence for a causal role of an agent so unusually defined took several years; dissent finally vanished as late as 1987.

Throughout May 1981, etiological clues were desperately needed to stop the spread of the disease. The distribution of hospital admissions was inconsistent with an infectious origin: no cases in children aged less than 6 months; no aggregation in hospitals, schools, barracks and underprivileged groups such as Gypsies; and resistance to treatment with antibiotics. Alert paediatricians first conceived the hypothesis of food poisoning. Over several weeks they had persisted in questioning the relatives of sick children about dietary habits: the use of illegal oil turned out to be common among children with the new syndrome and much less so in those hospitalized for other reasons. In the uncertainty prevailing at the time, these investigations – which some epidemiologists might consider crude – were carried out with a zeal and commitment reminiscent of John Snow’s search for clues to prevent the spread of cholera in London in the late summer of 1854.

An announcement by the Spanish Government on the role of the illegal oil on 10 June was followed by an official offer to exchange any suspect oil for guaranteed olive oil. This led to the creation of a bank of returned oils, sufficiently well organized to allow for the later identification of a number of containers of definitely case-related oils.

Case numbers started to subside in the second half of June, probably owing to both the Government’s announcement and a reduced availability of illegal oils in Spain.

Investigations
Achieving more satisfactory proof of causality relied exclusively on observational epidemiological studies. No experimental model for toxic oil syndrome has been identified, and all attempts to reproduce it in animals treated with case-related oils have failed. Similarly, little information has yet been obtained from laboratory attempts to mimic the procedures that had plausibly been used for illegally refining denatured oils.
An ad hoc national plan for toxic oil syndrome was soon set up. Since 1986, research has been coordinated by the Spanish Social Security Health Research Fund (FIS), in collaboration with the Centers for Disease Control and Prevention in the United States and under the supervision of a joint Committee of FIS and the WHO Regional Office for Europe. Epidemiological investigations passed through a number of phases.

Within several weeks of the first suspicion, case-control studies independently carried out in different areas consistently confirmed the strong association between toxic oil syndrome and the consumption of illegal oil. Their design allowed for unquantifiable misclassification of exposure, recall bias and limited comparability between cases and controls. None provided evidence of a dose–response relationship. With a couple of exceptions, these early studies were not reported in peer-reviewed literature, which limited the interest of the international scientific community in the episode.

For some years, epidemiological findings were descriptive: reports of individual or small series of cases occurring after the spring of 1981 and/or in remote geographical areas. In the end, it was found that everyone whose symptoms corresponded to the clinical definition of toxic oil syndrome had consumed illegal oil produced or bought in the spring of 1981. In a couple of convents, it was found that only residents dressing their salads with the illegal oil were affected. At a time when the causes of the disease were chaotically debated in the mass media, identifying, evaluating and unravelling apparent clusters of cases was not easy. The exclusion of alternative hypotheses (such as non-correspondence to the clinical definition of toxic oil syndrome or non-consumption of illegal oil) required even more skill, scientific rigour and time than usually demanded by the demonstration of any negative. Eventually, more formal proof of causality came from comparisons – in a case-control model – of the concentration of aniline-derived impurities among case-related and non-case-related oils stored in the oil bank “toxico-epidemiologic studies” (20).

The etiological and clinical uncertainties surrounding toxic oil syndrome induced alertness for the occurrence of clusters of clinically comparable conditions. “Eosinophilia-myalgia syndrome” appeared several years later, associated with the consumption of one particular brand of tryptophan marketed in the United
States. This syndrome does not show all the features of toxic oil syndrome, although its causes are as complex to understand. The point to emphasize, however, is that recent programmes developed jointly by the teams investigating both syndromes proved to be fruitful (21).

The clinical course of toxic oil syndrome deserved as much attention as its etiology. Exhaustive rosters of affected people were needed in order both to launch adequate prospective clinical studies and to ensure that attention was provided to everyone who needed it. In 1981/1982, the national plan for toxic oil syndrome compiled an official census of affected people to be used in programmes of financial compensation, social services and special medical care. At the time, diagnostic criteria for the syndrome may have not been consistently applied, so that the specificity of this census may have been lower than 100%. When FIS scientists started to design studies using this database, they were able to correct a sizeable number of errors and omissions by reviewing other medical files. The current (from 1985 onwards) version of the census includes over 20,000 people for whom a reasonably specific case definition of toxic oil syndrome has been verified. The sensitivity of the census is deemed satisfactory, on the basis of comparisons with lists of people requesting financial compensation and special medical care.

Results
Since 1981, clinicians have consistently reported severe chronic changes in toxic oil syndrome patients, such as peripheral neuropathy, hepatopathy, scleroderma and pulmonary hypertension. In spite of the availability of an adequate database of affected people, clinical and epidemiological investigations have been hampered by drop-outs, inconsistencies in physicians’ attitudes towards reporting, recall bias and the inadequacy of control groups used as standards in the estimates of prevalent conditions. Currently the tendency is towards a retrospective estimate of the bias introduced by these limitations and towards a retrospective standardization in the collection of clinical data. It is assumed that follow-up will allow the identification of excess cases of cancer, if any.

Confidence in the completeness of the census allowed an assessment of late mortality. In Spain, mortality databases do not
identify people by name. Thus, the deaths of people included in the census were retrospectively identified through direct contact with the families concerned and subsequently verified by other procedures. As yet, there is no evidence of any excess of late deaths, and findings (19) suggest decreased mortality among survivors of toxic oil syndrome as late as 1988; if confirmed, its interpretation will be complex but interesting. Analysing mortality by causes requires ad hoc studies on possible bias in death certificates.

**Conclusions**

This episode illustrates at least four issues in epidemiological studies following a chemical incident.

First, the biological plausibility of the only sustainable causal hypothesis was limited, but ad hoc studies centred on it turned out to be productive. The perception of the importance of apparently marginal, anecdotal episodes (such as the distribution of cases in convents) was crucial to the confirmation of causality. Equally crucial was, later, epidemiologists’ ability to design the “toxico-epidemiologic studies” (20) that formally provided proof of causality.

Second, in spite of the failure of experimental animal studies, the cooperation and exchange of ideas between toxicologists, chemists and epidemiologists has had a major role in the development of etiological knowledge. Over the years, the refinement of chemical analyses in the course of the “toxico-epidemiologic studies” has led to the retrospective identification of new substances in case-related oils, some of which may be candidate causes of toxic oil syndrome and worth being tested for toxicity in proper experimental systems.

Third, toxic oil syndrome, like other disasters, has probably modified individual lifestyles and interrelationships within the community, as suggested by the persisting decreased mortality, if confirmed. These aspects are as important and as difficult to investigate as more conventional etiological or clinical parameters.

Fourth, although the original goal of the victims’ associations was more related to civil rights than to epidemiology, the associations are taking part in a new dialogue in epidemiological research. This is most valuable for both the technical and the ethical aspects of investigations.
References
Chemical accidents can have serious and widespread effects on health. Epidemiology is an important tool for evaluating these effects and thus supplying information on which to base action to deal with a current accident and to help prepare for future ones.

Recognizing that epidemiologists can make a valuable contribution to each phase of a chemical incident – preparedness, response and follow-up – the WHO European Centre for Environment and Health convened a working group to set out some of the most effective approaches. This book is the result. It identifies the special part that epidemiology can play in a coordinated multidisciplinary response to a chemical incident, the tools to use in health risk assessment and roles in support activities such as training and the dissemination of information. The book supports and illustrates its arguments with lessons learned from the management of four major incidents in Europe: the fire at Schweizerhalle, the Seveso accident, the grounding of an oil tanker in Scotland and the toxic oil syndrome in Spain.

This book is directed specifically to the public health official or epidemiologist who may need to plan or undertake an epidemiological study of populations exposed to chemicals through major accidents or environmental contamination. Realizing the potential contribution of epidemiology to the management of chemical incidents is an important step in creating an effective multidisciplinary response.