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# **Assessing the value of epidemiological studies of acute chemical contamination incidents affecting drinking water**

*Final Report to the Department of the Environment*

DWI 4080  
FEBRUARY 1996



**ASSESSING THE VALUE OF EPIDEMIOLOGICAL STUDIES OF ACUTE  
CHEMICAL CONTAMINATION INCIDENTS AFFECTING DRINKING  
WATER**

Final Report to the Department of Environment

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# ASSESSING THE VALUE OF EPIDEMIOLOGICAL STUDIES OF ACUTE CHEMICAL CONTAMINATION INCIDENTS AFFECTING DRINKING WATER

## EXECUTIVE SUMMARY

Chemical incidents that result in the acute (i.e. short-term) chemical contamination of drinking water supplied to a substantial population of consumers are reassuringly rare. Such incidents provide the opportunity for epidemiological investigation to establish whether the contamination affected the health of the exposed population and, if possible, to quantify the effect, although there may be a number of other reasons for carrying out such studies. Before trying to decide whether epidemiological studies of acute chemical incidents should be encouraged, a view is needed on whether such studies are a) technically feasible and b) of value. With these questions in mind, the objective of this programme of research was to assess relevant published studies and establish the extent to which epidemiological investigations of acute incidents of chemical contamination have been or could be worthwhile. This included identifying requirements that future studies would need to meet to be regarded as useful.

In practice, there have been few epidemiological studies of the impact of contaminants on consumers who receive the water. Eleven studies were chosen for review and were assessed not only in terms of their technical quality but also whether they met their own declared aims and other specified objectives of particular interest to DOE.

The review demonstrated that epidemiological studies of acute chemical contamination of drinking water are technically feasible. Nine of these eleven studies were successful in investigating and quantifying the effects of the contamination on the exposed population. Only three of the studies, however, could be said to add to basic scientific knowledge on the toxicology of the contaminant involved. These three studies involved small populations and symptoms of illness that were susceptible to clinical confirmation. Eight of the studies were considered to have helped in the planning of the health care of the exposed population. All of the studies were considered capable of contributing to the management of any future incident involving the same or similar contaminants.

A number of weaknesses of varying importance were identified in the studies, although the review revealed two aspects that were critical for the quality of information that the studies were able to provide. These were a) the time interval between the onset of the incident and the start of the research; b) the provision of adequate information on the concentrations of the contaminant(s) in the drinking water to which members of the study population were exposed.

The report gives technical guidelines for future studies and makes recommendations of an operational nature. The two most important recommendations are, first, that contingency planning should be in place to establish a routine of good communication between all of the experts and organisations that need to be involved. Second, in order to ensure that adequate water sampling takes place to support an epidemiological study, resources must be available in addition to those already committed to the investigation and management of the cause of the incident. As one aspect of this, further consideration needs to be given to the storage of perpetual rolling samples at water treatment works.

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# 1. INTRODUCTION

Incidents that result in the acute (i.e. short-term) chemical contamination of the drinking water supplied to a substantial population of consumers are reassuringly rare. Such incidents are invariably followed by detailed investigation of the source of contamination and the reasons for failure to detect and prevent it entering the water treatment works or distribution system. These incidents also provide the opportunity for epidemiological investigation to establish whether the contamination affected the health of the exposed population and, if possible, to quantify the effect. Such epidemiological studies might be undertaken for a variety of reasons:

- to satisfy demands for action which may arise from the anger or concern of the exposed population;
- to assist in planning the health care of the exposed population;
- to generate basic scientific information on the toxicology of the contaminant;
- to contribute to the management of any future incident involving the same or similar contaminant;
- to provide evidence for use in legal action or the pursuit of damages.

In practice, there have been few epidemiological studies of the impact of contaminants on the consumers who receive the water. This may have been because major difficulties in planning, execution and interpretation were anticipated, or because it was difficult to overcome reporting bias when the effects or potential effects of an incident became public knowledge. Before trying to decide whether epidemiological studies of acute chemical contamination incidents should be encouraged, a view is needed on whether such studies would be a) technically feasible and b) of value. It is also important to consider what technical requirements need to be satisfied for an epidemiological study of an incident involving acute chemical contamination of drinking water to be regarded as successful.

With these questions in mind, the Department of the Environment (DOE) invited tenders for a programme of research to be managed by the Drinking Water Inspectorate (DWI). The objective of the research was to assess relevant published studies and establish the extent to which epidemiological investigations of acute incidents of chemical contamination of drinking water have been or could be worthwhile. This included identifying the requirements that future studies would need to meet to be regarded as useful. The contract was awarded to WRc and the findings are presented in this final report.

The first task was a literature search to discover what studies had been reported. A selection of these studies was then critically reviewed for their methodology, strengths and weaknesses, achievement of objectives and any lessons which could be learnt for the future. The findings of the review were used as a basis for suggesting guidelines for carrying out future epidemiological studies in similar circumstances.

This report is presented in two parts: the main body and the appendices. The main body of the report discusses the overall findings of the project including the selection of studies, the outcome of the review and the proposed guidelines for future studies. Appendix A contains detailed information on the results of the search and Appendix B contains the reviews of the selected individual epidemiological studies in turn.

## 2. LITERATURE SEARCH AND SELECTION OF STUDIES

### 2.1 Search

The first stage of the project was to locate reports on epidemiological studies that had investigated incidents of acute chemical contamination of drinking water. The original intention of this search was to cover world literature over the past 50 years. In practice, however, the sources of information available to us were not sufficiently comprehensive for this and their coverage was mainly of work published in English since about 1970.

Literature searches were made of WRc in-house sources and external on-line databases hosted by STN and DIALOG (e.g. Chemical Abstracts, Medline, Toxline and Waternet). Contacts were also made with a number of health authorities in the UK as well as the Scottish Centre for Infection and Environmental Health. Other bodies which were contacted included Health and Welfare Canada, the US Environmental Protection Agency (USEPA) and the US Centre for Disease Control (CDC). The CDC in collaboration with the USEPA has maintained a surveillance programme for the collection and periodic reporting of data on the occurrence and causes of waterborne disease outbreaks in the USA since 1971. The system relies on the state and local health departments voluntarily reporting the unusual occurrence of any disease and is therefore known to be subject to under-reporting. Although illnesses of microbiological and chemical origin are both investigated, it is recognised that chemical poisonings are less likely to be reported to CDC because they are not of an infectious nature.

The studies identified for potential review are listed in Appendix A. Only six studies were found in which large populations (>10,000) had been at risk of exposure. In these incidents, phenol (along with chlorophenols following chlorination) featured three times as the contaminant (Korea 1991; River Dee 1984 and Ufa, USSR, 1990). The three other studies involved different chemicals:

- i) a highly stable solvent which entered distribution via raw water contamination (UK, Worcester, 1994);
- ii) a water treatment chemical, aluminium sulphate, which entered the water supply through an operational error (UK, Lowermoor, 1988); and
- iii) the pesticide, chlordane, which was deliberately added directly into supply (USA, Pittsburgh, 1980). (This study was not, however, included in the set chosen for review, see Section 2.2).

The remaining incidents tended to involve much smaller populations (typically less than 1000 persons). In the USA, there were a number of incidents caused by operational error with on-site fluoridators which resulted in high fluoride levels in drinking water. Other

incidents were traced to contamination of the distribution system due to back siphonage or to some form of contamination occurring on the consumer's premises.

The country that featured most frequently in incidents of acute chemical contamination of drinking water was the USA. This is not necessarily because such incidents are relatively more common in the USA but is more likely to reflect the size of the USA and the more complete reporting of such incidents through the CDC.

Although there have been instances of acute health effects associated with contamination of drinking water by plumbing materials, notably copper, these have tended to affect only a few individuals within a single household. Incidents of this type were not included in the list nor were examples of illness associated with drinking contaminated water from isolated wells. In general, investigations of these incidents have identified the symptoms, analysed water samples and sometimes undertaken some form of clinical investigation. Where water analysis has revealed the presence of contaminants which are consistent with the pattern of illness, it has generally been concluded that the illness was due to drinking the water and corrective action was taken to improve the water supply.

## 2.2 Selection

The list of the studies identified for potential review was presented to DWI with brief details on when and where each study was carried out, the size of population at risk of exposure, the chemical involved and adequacy of information presented (Appendix A).

A short list of eleven studies was selected by DWI in consultation with WRc. The five incidents which involved the largest populations at risk of exposure were all selected for review. The remaining studies were selected on the basis of adequate details being reported, preferably in a published paper. These covered a range of chemical contaminants, different situations and varying methodological designs. The eleven studies are listed in Table 2.1

**Table 2.1 Epidemiological studies chosen for review**

Country/Region	Year	Chemical
1 Korea, Teagu City	1991	Phenol
2 UK, Dee	1984	Phenol
3 USSR, Ufa	1990	Phenol
4 UK, Worcester	1994	2-Ethyl-5,5-dimethyl-1,3-dioxane (EDD)
5 UK, Lowermoor	1988	Aluminium sulphate
6 USA, Alaska	1992	Fluoride
7 USA, New Jersey	1992	Nitrite
8 USA, New Mexico	1978	Fluoride
9 USA, Tennessee	1976	Chlordane
10 USA, Wisconsin	1974	Phenol
11 Canada, Ontario	1987	Nickel

### **3. REVIEW**

#### **3.1 Criteria**

A critical evaluation of the eleven selected studies was undertaken. Firstly, the methodologies of the different studies were evaluated and compared, and their strengths and weaknesses were identified from a technical viewpoint. The criteria for this review included:

- the length of time between the onset of the incident and the inception of study
- possible biases in the recruitment of subjects
- the estimation of individual exposure to the contaminant
- objectivity in the assessment of effects, including control for psychological influence
- establishment of base-line values against which responses were judged as abnormal
- allowance for age, pre-existing health status and other potential confounders
- appropriate statistical methodology and interpretation

The overall success of any epidemiological study can only be judged in relation to a declared objective. For the purposes of this review we included an assessment of not only how far the studies met their own objectives but also whether or not they met the following objectives set out by DWI:

- i) to establish whether the contamination affected the health of the population exposed;
- ii) to assist in planning the health care of the exposed population;
- iii) to generate basic scientific information on the toxicology of the contaminant;
- iv) to contribute to the management of any future incident involving the same or a similar contaminant.

Although it is recognised that a study may be undertaken to satisfy demands for action which may arise from the anger or concern of the exposed population, the success of meeting this objective could only be judged by undertaking surveys on public opinion and studying local media material relating to the event. This was outside the scope of this project as was the assessment of whether the studies provided sufficient information to be used in legal proceedings. However, it is recognised that public reassurance is extremely important and may in some instances be the driving force for a study to be undertaken.

### 3.2 Types and sizes of studies

Table 3.1 lists the eleven studies under review and outlines their principal features in terms of the cause of incident, the size of population at risk of exposure, the study objective and a general description of the study design or type.

**Table 3.1** Types and sizes of study

Study	Country	Year	Cause	Population at risk	Objective	Design/type of study
1 Teagu City	Korea	1991	S	2,000,000	E	Cohort
2 River Dee	UK	1984	S	2,000,000	E	Cohort
3 Ufa	USSR	1990	S	600,000	E	Cohort
4 Worcester	UK	1994	S	100,000	E	Cohort
5 Lowermoor	UK	1988	T	20,000	E	Cohort
6 Alaska	USA	1992	T	470	(E)	Cohort and case-control
7 New Jersey*	USA	1992	P	312	C	Case-control
8 New Mexico*	USA	1978	T/P	265	(E)	Total population
9 Tennessee	USA	1976	D	105	(E)	Total population
10 Wisconsin	USA	1974	S	26 households	E	Total population with external control group
11 Electroplating plant	Canada	1987	P	43	(E)	Total population

Notes:

- S = Source, T = Treatment, D = distribution, P = consumer's premise
- C = determine cause of the incident
- E = determine/quantify effects of the incident
- () = authors did not explicitly specify the study's objective
- \* = incident involved a school

The causes of the incidents varied and included contamination of source water (5 studies); operational error during water treatment (3 studies; two of these involved fluoride overdosing in the USA, one of which was due to operational error with an on-site fluoridator at a school). One incident was traced to a back-siphonage via the distribution system and 2 were caused by chemical contamination within the consumers' premises.

The first step in any study should always be to identify and state clearly the aims of the work. In four of the studies, the objectives were not explicitly stated by the authors.

Although it was relatively easy to guess what research questions were being addressed, it would have been more comforting if a clear statement had been made by the authors in the first place.

In ten of the eleven studies, it was known or strongly suspected at the start that chemical contamination of drinking water had taken place. In these studies the general objective was (or appeared to be) to try to confirm and quantify the possible health effects. For the remaining incident, the study was designed at a time when illness had been observed but the cause of the illness was unknown and the epidemiological study was intended to investigate the cause. This led to the adoption of a case-control approach, which allows a range of potential causes to be explored in a single study.

Three types of study emerged from the review. First, where the contamination involved a large population potentially at risk of exposure (i.e. thousands, millions), the studies were of a 'cohort' design, with health effects measured on a sample selected from the population. In this type of study, the cohorts or population groups are defined in terms of their degree of exposure to the contaminant. The term 'cohort study' in epidemiology usually carries a connotation that the study is longitudinal through time, involving successive measurements or continuous surveillance over a period. The studies considered in this present report only just satisfy this description. While in all cases there was a time interval between exposure and the assessment of effects, this assessment usually took place over a short interval of time and so some of the studies could almost be regarded as 'cross-sectional'. We have, however, retained the term 'cohort studies' to describe them because this term was used by several of the authors and is the most suitable for our purpose. The term is correctly used in the sense that the membership of the study groups was determined from information about exposure which would have been obtainable before any symptoms were manifest.

In most of these studies two groups were included, one from an area known to be supplied with water affected by the contamination (exposed) and one from an area known definitely not to have been supplied by water affected by the chemical contaminant (unexposed). Some of the studies included additional groups such as:

- a) a population from an area in which individuals thought they might have been exposed but were not;
- b) a population from an area in which individuals thought they had not been exposed to the contaminant but had in fact been exposed.

In these cohort studies, the study samples generally comprised hundreds of households and information was collected via self-administered postal questionnaires. Information on age, sex and health status was obtained as well as information on water consumption and on the symptoms individuals had experienced. This information was used to estimate the rates of symptoms of illness in exposed and non-exposed cohorts and these rates were analysed statistically to establish whether there was an association between illness and exposure. For all the incidents where the population at risk of exposure was >20,000 individuals, the epidemiological studies undertaken were of this design (Studies 1-5).

The second type of study which emerged was the 'case-control' design. This methodology was applied to the one incident where the cause of the illness was initially unknown (Study 7) and in one of the sub-studies of a fluoridation incident (Study 6). In these studies, individuals who met the criteria of having a defined illness (cases) were identified and individuals who did not have the illness/symptoms were designated as controls. Information on exposure in the cases and controls was obtained by administration of a questionnaire either by telephone or by personal interview. Statistical analyses were then applied to determine whether there had been significant differences in exposures between cases and controls.

For some studies under review, where the population at risk of exposure to the contaminated water was small (<300 individuals), it was possible to include the whole population rather than selecting a sample. These studies have been termed 'total population' studies, whether they were based on questionnaires or involved physical examination, clinical investigation or the analysis of biochemical samples.

### **3.3 Timing**

The time interval between the exposure of subjects and the investigation of effects varied widely (see Table 3.2). In general, the 'total population' studies and the case-control studies which involved small populations were initiated very quickly and certainly within a few days. The only exception to this was the Wisconsin study which involved pollution of a series of wells and where the temporal sequence of events was much slower than for an incident affecting piped water.

However, the time taken for the cohort studies to get underway had much wider variation ranging from 7 days up to 4 months. The study following the Worcester incident (Study 4) was the most rapidly initiated, which was one of the strengths of this study. In the case of the Lowermoor incident (Study 5), a time delay of 4 months occurred before the self-administered questionnaires were distributed. This must be regarded as a serious weakness.

It is important that the time interval between the onset of the incident and start of any epidemiological study investigating acute health effects (which may only last a few days) is as short as possible. There are two reasons for this. The first is that some types of information (e.g. samples of water and biological samples taken from the subjects) may become unavailable or useless if taken after the incident has passed. The second reason is that data held in human memory may be forgotten or incorrectly recalled. The latter is a strong possibility if the incident is accompanied by public anxiety or a high degree of media attention.

**Table 3.2 Timing of studies**

Study	Time interval between incident and survey
1 Teagu City, Korea	2 months
2 River Dee, UK	2 weeks
3 Ufa, USSR	(> 6 weeks)
4 Worcester, UK	7 days
5 Lowermoor, UK	4 months
6 Alaska, USA	≤ 7 days
7 New Jersey, USA	30 hours
8 New Mexico, USA	12 hours
9 Tennessee, USA	2-3 days
10 Wisconsin, USA	7 months
11 Electroplating plant, Canada	1 day

### 3.4 Recruitment of subjects

Table 3.3 gives information on the recruitment of subjects for the eleven studies including the sampling frame, response rate, achieved sample size and an indication of whether the method of recruitment would have ensured statistical independence (in a sense to be explained below).

In the cohort studies where populations were sampled, a number of different sampling frames were used (e.g. water consumer database, electoral roll and schools' rosters). In all cases the sampling frame was used to randomly or 'quasi-randomly' identify not individuals but households to which a number of self-administered questionnaires would be distributed. This method of recruitment could be described as 'cluster sampling' and there are likely to be correlations between the responses of individuals in the same family or, for example, children from the same school class. Consequently, individuals recruited within the same household cannot always be regarded as statistically independent when self-administered questionnaires are used. However, all the cohort studies did appear to treat the individuals recruited in this manner as statistically independent. In the Dee study (Study 2), the authors recognised that this was a difficulty but did not attempt to adjust the statistical analysis accordingly. The result of not making the appropriate statistical adjustment is that confidence limits are likely to be narrower than they should be. (We shall return to this point in Section 3.8).

In the two case-control studies, local clinic/hospital attendance records were used to identify cases. Controls were randomly selected from a sampling frame (e.g. school roster, addresses) containing the totality of individuals from which the cases had arisen. For

'total population' studies where the whole population at risk was included in the study, the method of recruitment was straightforward as sampling was not involved.

**Table 3.3 Recruitment of subjects**

Study	Sampling frame	Response rate	Resulting sample size	Independence of respondents
1 Teagu City, Korea	School pupils and family members	82%	5500	No
2 River Dee, UK	Electoral roll	69% (unexposed) 72% (exposed) 77% (exposed)	1200	No
3 Ufa, USSR	Unresolved	-	-	-
4 Worcester, UK	Water company's consumer database	56% (unexposed) 57% (unexposed) 65% (exposed)	3800	No
5 Lowermoor, UK	Water company's consumer database	43% (exposed) 46% (unexposed)	1000	No
6 Alaska, USA Case-control	Local clinic attendance and family members	Not stated	96	Yes
Cohort	Addresses	Not stated	175	No
7 New Jersey, USA	Local hospitals (cases); School roster (controls)	100% (cases) 59% (controls)	81	Yes
8 New Mexico, USA	Total population	78%	207	Yes
9 Tennessee, USA	Total population	100%	105	Yes
10 Wisconsin, USA	Total population	91%	158	Yes
11 Electroplating plant, Canada	Total population	100%	43	Yes

The response rate for the eleven studies varied quite widely. In the cohort studies the response rate ranged from 43% to 82%. The lowest response rate was for Lowermoor (Study 5) which was probably attributable to the time delay of 4 months between the incident and the distribution of the questionnaires. Following this particular incident, there was a loss of public confidence and this may also have influenced perceptions of the usefulness of the study and consequently the response rate.

For the other cohort studies, response rates were generally above 60%. The lower response rates of 56 and 57% related to residents from the control areas identified in the Worcester incident (Study 4), and slightly lower response rates were noted in unexposed groups than in exposed groups in some of the other cohort studies. In the Worcester incident, telephone calls from the unexposed area revealed that residents "did not see the need to reply as it did not affect their area" (Fowle *et al*<sup>(4)</sup>, 1994). In one of the case-control studies (Study 7) a lower response rate in the controls was apparent than the 100% response rate for the cases.

In an ideal situation, response rates of 100% would be desired for all the groups but in practice when using self-administered questionnaires, this is never achieved. Some studies included reminder letters with copies of questionnaires after a couple of weeks which did help increase response rates.

The whole population studies generally had good response rates, ranging from 78 to 100%. This is probably a reflection of the small size of the population at risk and the fact that personal or telephone interviews were undertaken as opposed to use of self-administered questionnaires.

### **3.5 Exposure estimation**

Table 3.4 lists the information that was gathered for estimating exposure. In general this involved i) analysis of water samples to estimate how much of the chemical was supplied in the contaminated water and ii) obtaining information on water consumption by individuals. The water consumption data which were obtained from individuals could be categorical or quantitative. Categorical data only involved ascertaining whether water was consumed or not, whereas quantitative data also included information on how much water was consumed. In the report of some studies, details were lacking as to exactly what information was obtained, although it must have been at least categorical.

The number of water samples taken to estimate the concentration in water varied widely. In the case of the incidents which involved large populations at risk with the contaminant present in distribution, the number of samples on which the exposure estimates was based were largely inadequate. For example, in the Dee incident (Study 2) exposure estimates were based on only 2 water samples (although it was unclear in the published paper that the quoted results were extrapolated rather than measured concentrations). In the paper reporting on the Korean incident (Study 1), only 1 distribution sample was mentioned. It may have been that more water samples and analytical data were available than were reported in some of these papers but, if so, there is no excuse for their omission. In at least four of the major studies (1-4), the lack of environmental data on which to estimate exposure is a serious flaw. In some of the studies, it was suggested that the peak level of contamination was likely to be higher than those reported but water samples were not available for analysis to confirm whether this was the case.

**Table 3.4 Information gathered for estimating exposure.**

Study	Concentration measured in water	Number of contaminated water samples taken.	Water consumption information
1 Teagu City Korea	Yes, but poor explanation of data. (likely to be underestimated)	7 (6 of which related to 2 service reservoirs; only 1 was a distribution sample. Samples were taken on 4 consecutive days).	Not clearly stated. Categorical at least.
2 River Dee, UK	Yes, also involved extrapolation of results. (likely to be underestimated)	2 (1 service reservoir and 1 tap sample. Additional results were presented in the Lancet paper but these were extrapolated analyses. Analysed for phenol and chlorophenol).	Categorical.
3 Ufa, USSR	Yes, poor details	Not stated	Categorical and quantitative questions included in draft questionnaire
4 Worcester, UK	Yes	2 (distribution samples and peak levels reported in paper, further samples were taken by the water company).	Categorical and quantitative.
5 Lowermoor, UK	Yes	1 (peak level reported in outlet sample in paper; more samples were taken by the water company)	Categorical and quantitative.
6 Alaska, USA	Yes	Not stated (single average value assumed)	Categorical and quantitative
7 New Jersey, USA	Yes	Not stated (tap samples)	No, food consumption history
8 New Mexico, USA	Yes	2 (water fountains)	Categorical and quantitative
9 Tennessee, USA	Yes	42 (individual household samples)	Yes, but details lacking
10 Wisconsin, USA	Yes	45 (individual well samples)	Categorical and quantitative.
11 Electroplating plant, Canada	Yes	1 (water fountain)	Yes, but details lacking

It is interesting to note that in two of the total population studies (9, 10) which involved contamination of a water supply to a relatively small number of households, water samples were taken for each household. In the case of study 9, the concentration of chlordane in the water supplied to the 42 individual households varied from 0.1 to 39,800  $\mu\text{g l}^{-1}$ . This illustrates the effect of mixing in distribution. By taking water samples at individual households, much more reliable estimates of exposure could be achieved.

In situations where the water contamination occurred at the consumers' premises and involved a single source of drinking water such as a 'water fountain' or 'tap', analysis of only a few samples or even a single water sample may be adequate to estimate exposure. In this case the assumption of the chemical contaminant being fully mixed is valid. However, more than one sample would still be needed to estimate concentration throughout time.

### **3.6 Measurement of effects**

Table 3.5 gives information on the measurement of adverse health effects. The studies involving large populations at risk (Studies 1,2,4,5) all used self-administered questionnaires which obtained information on the occurrence of various symptoms. None of these studies included any biochemical measurements or sought confirmation by clinical diagnosis. All of the cohort studies obtained information about pre-existing illness except that of the Dee incident (Study 2).

Where the self-administered questionnaires were available for review, these were of good design, especially the one used at Worcester. Some of the questions in the draft questionnaire for the Ufa incident required rather detailed answers from the respondents which may have been a little ambitious in view of the likely time interval (at least 6 weeks) before the questionnaires would be administered. In the preliminary report on the Ufa incident, although the draft questionnaire was included, the way in which it was to be administered appeared to be unresolved. There seemed to be two possible methods a) self-administered questionnaires being sent to households or b) interviews with doctors either by house visits or by individuals visiting polyclinics.

The remaining studies which involved much smaller numbers of subjects did not use self-administered questionnaires, but interviews either over the telephone or by personal visits. These studies tended to have higher response rates than those using self-administered questionnaires. In all of these studies individuals were asked about their symptoms but in five of the studies (6,7,9,10,11), blood and/or urine samples were also taken and biochemical measurements made. Three of these studies also ascertained clinical diagnoses.

In the studies under review, the decision to undertake biological sampling appeared to be dependent on the size of the population at risk, the situation of the incident and to some degree on the chemical contaminant, its concentration in the water and the toxic effects which were observed. For example, when the contamination incident involved a factory,

biological sampling and physical examination were rapidly initiated which was probably a reflection of the health and safety planning procedures in place (Study 11).

In incidents involving chemicals where a toxic-endpoint can be quantified by biomarkers in the blood or urine, biological sampling can be very useful. For example, in the incident which involved nitrite (Study 7), cyanosis was observed as a result of methaemoglobinemia. The levels of methaemoglobin measured in blood were used as a 'biomarker' for the toxic effect and cases were selected on this basis. In the Alaska incident which involved high levels of fluoride entering supply, serum levels of lactate dehydrogenase, phosphate and magnesium were measured to determine whether acute systemic effects had occurred (e.g. cell damage, imbalance of mineral homeostasis).

**Table 3.5 Measurement of effects**

Study	Method	Symptoms (number)	Clinical diagnosis	Biochem measure.	Data on pre-existing illness
1 Teagu City, Korea	Saq	Yes (14)	No	No	Yes
2 River Dee, UK	Saq	Yes (7)	No	No	No
3 Ufa, USSR	(Q)	Yes (20)*	-	-	Yes*
4 Worcester, UK	Saq	Yes (13)	No	No	Yes
5 Lowermoor, UK	Saq	Yes (18)	No	No	Yes
6 Alaska, USA	I	Yes (11)	No	Yes	No
7 New Jersey, USA	TI	Yes	Yes (cases)	Yes (cases)	No
8 New Mexico, USA	TI	Yes	No	No	No
9 Tennessee, USA	I	Yes	No	Yes	No
10 Wisconsin, USA	I	Yes (14)	Yes (Phys.)	Yes	No
11 Electroplating plant, Canada	I	Yes	Yes (Phys.)	Yes	Yes

Notes:

- - = Unclear
- Saq = Self-administered questionnaire
- I = Interview
- TI = Telephone interview
- (Q) = Questionnaire, method of administration not known.
- Phys. = Physical examination
- \* = Based on draft questionnaire

For the chlordane incident (Study 9) which involved relatively large concentrations of the contaminant in the drinking water, chlordane metabolites were measured in serum samples to help determine to what extent individuals had been exposed. This is an example where biological sampling was useful for estimating exposure. This was also true of the Alaska (Study 6) and electroplating (Study 11) incidents where urine/serum levels of fluoride and nickel, respectively, were measured to estimate the extent of exposure. In both cases, relatively large concentrations of the contaminant had been present in the water.

Such biological sampling would have been useful in the Lowermoor incident to determine to what extent exposure had occurred by measuring blood and urine aluminium levels. However, to be helpful this would have had to be done extremely quickly and it would have been no use at all four months after the incident.

Although biological sampling can provide a more objective assessment of exposure and toxic effects, it should be recognised that it will not necessarily be helpful in all incidents. For example, biological sampling would not have been particularly helpful following the Worcester incident. Firstly, there were no toxic end-points reported in this incident for which 'biomarkers' could have been used. Secondly, the concentration of the contaminant in the drinking water was so low ( $\text{ng l}^{-1}$  levels) that biological monitoring would not have provided a sufficiently sensitive index of exposure.

### **3.7 Control for psychological influence**

Table 3.6 provides information on whether the studies tried to control for the effects of psychological factors caused by the incident that might have been confused with direct toxic effects of the contaminant.

For acute toxic symptoms such as cyanosis, which can be confirmed by physical examination or biological sampling, the issues of psychological potentiation become redundant. However, when the symptoms are 'soft' toxic endpoints which are common (e.g. headache, nausea and gastrointestinal symptoms), it is difficult to determine whether these are related to direct toxic effects of the contaminant or to psychological factors. It is extremely difficult to control for such effects, but there are some steps which can be taken to determine if the toxic effects observed can be related directly to the chemical contaminant.

Such steps include the use of:

- a) additional subjects who do not know their exposure status.
  - In the case of cohort studies, in some circumstances it may be possible to include additional subjects who think they have been exposed to the contaminant but have not and visa-versa. These subjects can then be compared with those who are known to be exposed and unexposed and analysed to determine if there is any effect on the prevalence of reporting of

symptoms. (Study 4 did this, whereas Study 1 collected the necessary data but failed to analyse it).

b) Dummy symptoms

- Symptoms that are unrelated to the expected toxicity of the contaminant can be incorporated in questionnaires in order to detect exposed individuals whose symptoms could be of psychogenic origin. For example, in two of the incidents involving phenol, the prevalence of 'fever', which would not be expected to be associated with acute phenol poisoning, was determined. If the prevalence of such an unrelated symptom were significantly increased in the exposed group, then it might point to a psychogenic effect. Also, in the Lowermoor study, information for 20 symptoms including 'some not related to acute aluminium toxicity', was obtained. The prevalence of each symptom was increased in the exposed group, which would suggest a degree of psychogenic influence. When using dummy symptoms to rule out psychogenic effects, it is important not only to state that this was done, but also to indicate what the dummy symptoms were.

c) Awareness of exposure

- Most of the studies asked whether individuals could detect an unusual taste, smell or appearance of their water. This information can be analysed to try and address whether there was an association between the prevalence of symptoms and whether an individual could detect something unusual about the water i.e. awareness of exposure. For example, in the Worcester study (Study 4), the authors analysed whether the fact that consumers could detect an odour or taste was related to their symptoms. This question was also addressed in the Dee incident. In the Korean study, the authors asked individuals not only about whether an unusual taste or odour was detected in their water but obtained information about awareness of exposure through an individual's knowledge of his/her water supply. However, disappointingly, the authors did not actually analyse these data to determine what differences, if any, the awareness of exposure may have made to the responses given.
- The most important way that consumers can be made aware that their drinking water may be contaminated is by being officially told not to drink it. In some of the large incidents consumers were so advised (Studies 3,4) but in others not (Studies 1,2,5). It is important to take this into account in interpreting the results of the studies. In all of the smaller studies actions were taken which ensured that the contaminated supply was turned off.

Our discussion of the possible role of psychological effects has so far rested on the assumption that the responses of the subjects were biased inadvertently rather than deliberately. It is conceivable that in some situations, where there is particular animosity to the water company or where there is a hope of compensation for injury that individuals may be tempted to greatly exaggerate exposure or symptoms. While we have no concrete evidence that this has actually happened or could significantly affect an investigation, it would be prudent to bear the possibility in mind when planning a study.

**Table 3.6 Methods for controlling psychological influence.**

Study	Additional cohorts	Inclusion of dummy questions	Measurement of awareness of exposure to contaminated water
1 Teagu City, Korea	Yes, depending on knowledge of water supply. Not analysed.	Yes	Yes (taste/odour)
2 River Dee, UK	No	No	Yes (taste)
3 Ufa, Russia	Yes (planned)	Yes*	Yes (taste/odour)*
4 Worcester, UK	Yes, additional cohort included who thought they may have been exposed but were not.	No	Yes (taste/odour)
5 Lowermoor, UK	No	Yes, but not stated what they were.	Yes (taste, colour)
6 Alaska, USA	No	Not stated.	No
7 New Jersey, USA	Not applicable	Not applicable	No
8 New Mexico, USA	Not applicable	Not stated	No
9 Tennessee, USA	Not applicable	Not stated	No
10 Wisconsin, USA	Not applicable	Yes	No
11 Electroplating plant, Canada	Not applicable	No	No

\* based on draft questionnaire

### **3.8 Statistical analysis**

The features of the main statistical analyses of the selected studies are summarised in Table 3.7. In all cases we have taken the 'main statistical analysis' to mean the attempt to quantify or test a relationship between some measure of exposure to the contaminant and some measure of possible effects. We have included relationships involving biochemical measurements; such measurements can be viewed as markers of exposure relating either backwards to the intake of the contaminant or forwards to a toxic endpoint.

When reading Table 3.7 it is important to note that the entries describe the analyses that were actually reported, not the analyses that might have been done on the data that were collected (Tables 3.4-3.6). Thus, for example, Studies 9 and 10 included water samples taken from individual households but these were not used in any formal analysis of the measured health effects.

### **Estimation of exposure**

The first three columns of the table indicate how the analyses dealt with estimation of exposure. Although the categorical treatment (e.g. high, low; exposed, unexposed) of exposure fits well with the 'cohort' design, it was disappointing to find that none of these studies had treated concentration as a quantitative variable, not even the three studies (6,9,10) where quantitative information had been collected. Three of the studies (4, 5 and 6c) did make use of quantitative information to describe the volumes of contaminated water consumed by individuals. Most of the studies, however, treated volume consumed only in a categorical way (e.g. some, none) in which case the combined assessment of intake (concentration x volume) must be categorical also.

The next three columns of the table describe whether or not the studies included certain features that might be considered desirable to ensure fairness of comparison, statistical validity or sharpness of inference. The relative importance of these features does, however, depend very much on the circumstances of each case.

### **Adjustment for age**

Only two of the studies incorporated formal adjustment for age (Studies 4 and 7). Such adjustment is important in epidemiological studies where the potential confounding effects of age have not been adequately controlled in the study design. In two studies (1 and 2) enough information is given to show that age adjustment was not needed. It is, however, less easy to reach this conclusion in Study 5 where the data indicated a need for age adjustment, but none was performed.

### **Allowance for pre-existing illness**

Three studies (1,4,5) considered the need to make allowance for the health status of the subjects before the onset of the incident. In one study (4), the cohorts appeared to be balanced in this regard and no further action was taken. The other two (1,5) circumvented the difficulty by excluding subjects with pre-existing symptoms. This is an acceptable way of dealing with the issue in studies of this type but it is not the only way. The other studies collected no information on pre-existing illness and so it was not possible to take it into account. The seriousness of this omission depends to some extent on the effect or 'end-point' being investigated. For unusual or highly specific end-points e.g. methaemoglobinemia (Study 7), the allowance may be judged irrelevant, but for common

**Table 3.7 Features of main statistical analyses**

Study	Treatment of exposure			Adjustment for			Formal statistics	
	Concentration	Volumes consumed	Combination	Age	Pre-existing symp.	Awareness (taste or odour)	Quantities analysed	Statistical method
1	Categorical	Categorical	Categorical	Not needed	No	No	Attack rates	$\chi^2$
2	Categorical	Categorical	Categorical	Not needed	Yes	Yes	Attack rates	$\chi^2$ and Fisher's exact test
4	Categorical	Quantitative	Quantities within categories	Yes	Not needed	Yes	Attack rates	$\chi^2$
5	Categorical	Quantitative	Quantities within categories	No	Yes	No	Attack rates	Confidence limits for relative risk and proportional risk
6	Categorical	Quantitative	Quantities within categories	No	Yes	No	Attack rates	Confidence limits for relative risk and proportional risk
Case-on. Cohort	Categorical	Categorical	Categorical	No	No	No	Odds ratio	Confidence limits
Biochem.	Categorical	Categorical	Categorical	No	No	No	Attack rates	Confidence limits for relative risk
7	Single value assumed	Quantitative	Quantitative	No	No	No	Serum F	Correlation coefficients
8	Categorical	Categorical	Categorical	Yes	No	No	Urine F	Confidence limits
9	Not considered	Not considered	Not considered	No	No	No	Odds ratio	$\chi^2$
10	Not considered	Not considered	Not considered	No	No	No	Attack rates	Geometric means, confidence limits
11	Categorical	Not considered	Not considered	No	No	No	Metabolites in serum v illness	Fisher's exact test
	Single category	Categorical	Categorical	No	No	No	Attack rates	Fisher's exact test
				No	No	No	Serum/urine Ni.	Means, Stand. errors

or non-specific endpoints (e.g. abdominal pain), adjustment for previous occurrence may be more important.

### **Inclusion of information on awareness of contamination**

Information on whether subjects were aware that their water had been contaminated can help disentangle the overlapping effects of toxicity and anxiety. Four of the large studies (1,2,4,5) collected information of this kind but only two (2,4) made use of it to modify their analysis in a way that would help to clarify the potential influence of psychological effects.

### **Allowance for clustering of responses**

None of the large scale studies based on self-administered questionnaires (1,2,4,5) made formal adjustment or allowance for the clustering that could have arisen from their methods of recruitment when combined with possible non-independence of responses supplied by members of the same family. In theory this is a serious criticism because it casts doubt on the assumption of independence on which the analysis of the studies depend. In practice, the impact of this criticism is likely to be small but unfortunately, from the information given, it is impossible to be sure.

Methods are available for coping with this difficulty (Cochran 1977) and their use in market research would be regarded as standard. These methods would, however, be rather less attractive in the present type of epidemiological study. Better advice would probably be to use a sampling frame that avoids the difficulty in the first place. This issue is much less important in the studies where questionnaires are administered by an interviewer, and still further in studies where the health effects are defined in terms of 'hard' end-points. The criticism was therefore considered as not applicable to Studies 6-11.

### **Technical method applied**

The last two columns of the table describe the variables analysed and technical methods used. These methods can all be regarded as standard and in all cases appear to have been correctly applied.

## **3.9 Interpretation**

Comments on the authors' interpretation of each of the studies are given in the commentary sections Appendix B. For most of the reports we found ourselves in general agreement with the conclusions the authors had drawn. There were, however, three exceptions to this, where we tended to disagree with the authors' attribution of cause of the effects observed. The three exceptions involved the difficult area of distinction between genuine toxicity and symptoms that might have been induced psychologically.

With the Korean study we simply disagree with the authors' claim that their analysis was able to "rule out psychogenic effects". Almost the reverse problem arose in the Worcester study. Here, the authors' interpretation attributed the observed increase in symptoms rates not to the degree of contamination itself but to the customers' ability to detect the unusual taste or smell. We do not accept that the information presented was enough to support this contention. In the study of the incident in Lowermoor the authors designed their analysis to compensate for the possibility of psychologically induced effects but the excess reports of joint pains (i.e. in proportion to total symptoms) in the exposed area could fairly easily be attributed to chance. The authors' conclusion here would be sustainable only if the excess joint pains had been specified as an important hypothesis in advance of the results being seen, or if a much higher level of significance had been achieved.

### **3.10 Achievement of objectives**

Table 3.8 lists whether the studies met their own declared objectives and the four specific objectives of interest to DWI:

- |            |  |
|------------|--|
| DWI (i):   | To establish whether the contamination affected the health of the population exposed:              |
| DWI (ii):  | To assist in planning the health care of the exposed population:                                   |
| DWI (iii): | To generate basic scientific information on the toxicology of the contaminant; and                 |
| DWI (iv):  | To contribute to the management of any future incident involving the same or similar contaminants. |

All of the studies met their own objectives or at least achieved this in part. It can be said that most studies met DWI's primary Objective (i), although Lowermoor (Study 4) failed even to do this. We declared three of the studies to have failed to meet Objective (ii), mainly as a result of the time delay.

Only three of the studies could be said to generate basic toxicological data about the contaminants (Objective iii). In all cases these were small studies in which biological monitoring had been undertaken, involved 'hard' toxic endpoints and an estimation of the doses which were associated with symptoms. However, the incompleteness of the reporting in a few of the studies was rather disappointing in view of the detailed biological and environmental sampling which had been done (e.g. Studies 9 and 11). This limited the extent of the toxicological findings that could have almost certainly been gained but were not reported in the published papers.

All studies met Objective (iv) which was to help assist in the planning of future incidents. This was not only because of the positive features which were identified in some of the studies but also because lessons could be learnt from weaknesses.

**Table 3.8 Achievement of objectives**

Study	Own	DWI (i)	DWI (ii)	DWI (iii)	DWI (iv)
1 Teagu City, Korea	Yes	Yes	No	No	Yes
2 River Dee, UK	Yes	Yes	Yes	No	Yes
3 Ufa, USSR*	(Yes)	(Yes)	No	(No)	(Yes)
4 Worcester, UK	Partly	Yes	Yes	No	Yes
5 Lowermoor, UK	Partly	No	No	No	Yes
6 Alaska, USA	(Yes)	Yes	Yes	Yes	Yes
7 New Jersey, USA	Yes	Yes	Yes	No	Yes
8 New Mexico, USA	(Yes)	Yes	Yes	No	Yes
9 Tennessee, USA	(Partly)	Yes	Yes	Partly	Yes
10 Wisconsin, USA	Yes	Yes	Yes	Yes	Yes
11 Electroplating plant, Canada	(Yes)	Yes	Yes	Yes	Yes

() means we do not really know since the authors did not state their own objectives or we do not have the relevant information

\* Hypothetical since the report was of a preliminary nature which only suggested the type of epidemiological study necessary.

### 3.11 Deficiencies and difficulties

The schedule of work for this project particularly asked for the contractor to comment on deficiencies identified in the studies and on difficulties encountered with their conduct. These matters have been dealt with in detail in Appendix B and in a general way in Sections 3.3-3.8. The purpose of this section is to highlight the most important points, which have seriously limited the effectiveness of the studies. Amongst the deficiencies the most important have been:

1. Objectives not explicitly stated;
2. Too long a time interval between the exposure and crucial measurement of effects;
3. Inadequate sampling of the relevant drinking water, leaving uncertainty over the concentrations to which people were exposed;
4. Low response rates in population surveys;

5. Ineffective distinction between toxic and psychogenic effects;
6. Results not fully analysed and reported.

While these deficiencies emerge fairly clearly from the review, the difficulties encountered in conducting the studies are perhaps less obvious and more subject to speculative judgement. The difficulties appear to be of two different types; which could be described as administrative and technical.

On the technical side one severe difficulty must have often have been the lack of prior information about the nature and size of the effect(s) that the study is attempting to measure. This has consequential difficulties particularly for the design of the study. Those studies which were based on sample surveys of the general population also encountered difficulties in the areas indicated by deficiencies (4) and (5) mentioned above. These technical difficulties were, however, perhaps less important than some of the difficulties of an administrative nature:

- a) It was not always clear who was responsible for initiating and executing the study. This observation would probably have been made with greater force if we had reviewed some incidents after which studies did not take place.
- b) The relevant agencies have often lacked the preparedness to initiate studies within appropriate time.
- c) Both the conduct and authorship of some of the studies indicate that communication between experts in different but relevant fields has been less than ideal.

## **4. GUIDELINES FOR FUTURE STUDIES**

The strengths and weaknesses identified in the eleven studies have formed the basis for the guidelines for future epidemiological studies. These guidelines have been divided into two areas a) technical, where guidance is given on how to carry out such studies and b) operational which deal more with planning for such studies and the procedures to have in place.

### **4.1 Technical**

#### **Design of study**

The decisions about the study design will depend on the circumstances of the incident, the purpose of the study and its objectives. A clear statement of objectives is essential as a basis for rational design.

Although no single design of study can be recommended for all circumstances, a number of points can be made:

- a) In outbreaks of illness where the cause of the incident is unknown, the preferred approach is usually to use a case-control design. For example, this method is generally adopted when investigating outbreaks of illness which are consistent with microbiological aetiology to establish if the cause is waterborne rather than related to another route e.g. food contamination.
- b) In incidents where the cause of illness is known to be related to chemical contamination of water, a cohort design is likely to be the best approach to try and confirm and also quantify the effects.
- c) If the population at risk of exposure is small, it may be possible to include the whole population in the study, perhaps with an unexposed population living nearby.

#### **Timing**

Whatever design of study is chosen, the study will be much more effective if it is quick off the mark. This is one of the most important recommendations when carrying out studies investigating acute incidents in which the pollution itself and its possible effects may last only a few days. If a study is rapidly initiated this will not only mean that appropriate environmental sampling and biological monitoring can be carried out, but it will also reduce the possibility of information being incorrectly recalled. Studies that are rapidly undertaken will also be more successful in maintaining public confidence and are less likely to be adversely affected by the media. Indeed, the media can have a strong influence on the success of a study and steps should be taken to involve them at the outset if at all possible. The only sure way in which epidemiological studies can be undertaken rapidly

will be to have contingency plans already in place (see section 4.2. for operational guidance).

### **Recruitment of subjects**

For studies in which members of the population are recruited by sampling, the sampling frame will need to be considered. Although this will depend on the circumstances of the incident, contingency planning should be carried out to establish feasibility and guidance on choice of sampling frame. Examples of sampling frames which can be used include;

- a) Residential addresses
- b) Electoral roll
- c) Water company's billing database
- d) GP age-sex registers (Details such as age, sex and address are included in these records. However, ethical approval will be needed to use these records and therefore a procedure should be in place for obtaining this rapidly otherwise the study may be delayed).

Statistical guidance also needs to be available on the size of the sample that should be selected, and the way in which this size is linked to the objective of the study. At the same time the method of choosing the sample needs to be carefully considered. In the studies in which a number of individuals were recruited from the same household (cluster sampling), the subsequent statistical analyses failed to allow for the problem that responses should not be treated as statistically independent. One way to overcome this possible dependence is to use a different sampling frame. Alternatively, it is possible to make an appropriate allowance for clustered responses at the time when the data are analysed. Clustered sampling should be undertaken only by research teams who are capable of implementing this.

An inherent difficulty in using postal questionnaires is that the response rate can be poor and uneven in different groups. This can sometimes be related to the timing of the study, which re-emphasises the need to avoid delay in starting the study. It may, however, be appropriate to consider alternatives to postal questionnaires e.g. telephone or personal interviews. However, if postal questionnaires are being used one way to increase response rates is the distribution of postal reminders.

### **Exposure estimation**

#### Concentrations

The need for adequate water samples to be taken to estimate exposure needs particular attention. Water companies will be familiar with their distribution system and would be most appropriate to undertake the water sampling. In some instances, more water samples and analytical data may have been available than were reported in the published papers.

Such a possibility highlights the importance of communication between water scientists and those undertaking the epidemiological study to ensure that all water sampling data are available on which to base exposure estimates.

In an incident the number of water samples required for the purposes of estimating exposure for an epidemiological study may exceed that required for operational purposes. Furthermore the objective of sampling is quite different. Therefore, contingency plans should be in place so that when an incident occurs additional sampling is taken at points likely to be representative of the water received.

In some of the reviewed studies, it was suggested that the peak level of contamination was likely to have been higher than that reported, but that water samples were not available for analysis to confirm whether this was the case. This difficulty could only be overcome by keeping water samples entering supply from the water treatment works on a perpetual 'rolling' basis. The time period for which these samples would need to be kept would depend on the size of the distribution system. No analysis need be undertaken on such samples during normal operations but their retention would ensure that, should an incident occur, relevant water samples would be available for analysis.

Both the above suggestions would require extra resources to be available in addition to those needed for operational purposes. For additional sampling following an incident the additional resources would need to be made available only at the time. For perpetual rolling sampling at the treatment works the resources would need to be permanently in place.

### Quantities

For all subjects that are included in the study it is important to obtain information about the quantities of water consumed from the contaminated source, from alternative sources, and the way in which these quantities changed during the course of the incident.

### **Methods of assessment of effects**

The methods of assessing effects will depend very much on the incident, chemical involved and concentrations in the contaminated water. There are a number of ways in which effects can be assessed including:-

- a) Clinical diagnosis (based on symptom history, physical examination and clinical investigation)
- b) Biological sampling (blood and/or urine)
- c) Interview (telephone or personal)
- d) Self-administered questionnaires.

In choosing which of the above is appropriate, it will be essential to consider what are the likely health effects. Expert toxicological advice is likely to be needed at this stage. For

example, it would be useful to know whether there are any expected toxic effects for which some form of 'biological marker' could be measured in biological samples to quantify toxicity. On the other hand, the expected toxic effects may be indicated only by subjective symptoms e.g. headaches, nausea. For these, there are no biomarkers available to quantify the toxic effect and biological sampling will be of limited value for this purpose.

A second reason for biological sampling is to help quantify personal dose. This can potentially be very useful. However, its feasibility and the decision as to whether this would generate useful information will be highly dependant on the chemical and the concentration involved in the incident.

The need for biological monitoring therefore should be considered in any contingency plan. In large cohort studies, where it be impractical to biologically monitor all individuals, useful information may be gained by carrying out biological sampling on a random sub-sample of the population. The final decision on whether biological monitoring will be of use will depend on the nature of the incident, the identity of the chemical contaminant and the concentrations involved.

Where possible, it is better to base a study on objective clinical or biochemical effects and avoid 'soft' end points. The use of 'soft' end points can make it very difficult to distinguish toxic from psychogenic effects. However, this can be mitigated to some extent by certain steps and the following should be considered in the design of a study;-

- inclusion of 'dummy symptoms' alongside the expected toxic responses;
- questions about awareness of exposure; and
- use of additional subjects who might have thought that they had been exposed when in fact they were not.

If self-administered questionnaires are to be used, it will be important that they are not too complicated or lengthy. They should normally include questions on demographic information, confirmation of exposure status, incidence of symptoms, awareness of exposure and pre-existing illness. The wording of the covering letter is important since it can influence the response rates and should include information about the investigative agency and the reasons for doing the study. As part of any contingency planning it would be prudent to have an outline structure for a questionnaire already prepared in order to reduce delays in starting the study.

### **Statistical analysis and reporting**

The statistical analyses were generally satisfactory in the studies under review, apart from the lack of adjustment for clustered responses in the cohort studies. The main potential improvements in statistical analysis and reporting mainly depend on improvements in the design of the studies and on the full exploitation of the information that has been collected. This includes adjustment for covariates, such as age, where appropriate. It is

important that all data should be analysed and reported, or the reasons for not doing so should be given.

### **Summary of important requirements**

- a) Study must have a clear objective.
- b) Start the study as soon as possible to allow its objective to be achieved.
- c) Ensure that there is a large enough number of subjects to meet the study objective.
- d) Include adequate water sampling and information on quantities consumed.
- e) Base on 'hard' endpoints and include biological monitoring wherever possible.
- f) Take account of consumers 'awareness' of exposure (taste/odour; whether or not they thought they were in the affected area; whether or not they complied with advice not to drink).
- g) Include adjustment for pre-existing conditions and age.
- h) Give appropriate statistical analyses and report fully.

## **4.2 Operational**

Incidents involving chemical contamination of drinking water supplied to large populations are rare. The rarity of such events will tend to mean that the person dealing with an incident will not have previous experience. Emergency contingency plans for dealing with such acute chemical incidents are therefore strongly recommended.

Any contingency plan should have a designated individual who will be responsible for deciding whether or not an epidemiological study should take place and for the execution of the study. In the health authority, the designated individual is often the local consultant in communicable disease control (CCDC) but a deputy should be also nominated. Furthermore, there should be designated staff to join the management team of the study and any contingency plan should identify a mechanism for mobilising this team (e.g. list of contacts, telephone numbers, pager numbers).

A key feature of any contingency plan should be to establish good communication between all experts/organisations identified and listed by name in the plan. For example, for an incident involving drinking water, it is essential to communicate fully with the water supplier and to have established good links prior to an incident taking place. Ideally individuals should also be familiar with the different organisations from which they can obtain medical, toxicological, chemical, sampling and statistical advice.

In order to ensure that there are no large gaps in any contingency plan, at least the communication links should also be tested in an 'emergency exercise'. Also, it must be regularly reviewed and updated.

The contingency plan should contain information on the following:

- Information on the water supply companies within the area (contact numbers, the areas of supply). Contact names of water scientists within the company should also be included in order to gain information on how the chemical contaminant will behave during water treatment and in the distribution system.
- Information on who to contact for toxicological advice. This may include a local network of experts as well as other organisations and details such as names and contact numbers should be included. A brief description of the organisation/expertise may also be helpful. It would also be important that appropriate measures have been taken to ensure that such expertise can be made available. Examples of organisations which can provide advice include:-
  - Health Advisory Group on Chemical Contamination Incidents (HAGCCI), DOH. This is an expert advisory group that was established following the Lowermoor incident and which can be contacted through the DOH to give advice following major chemical incidents involving drinking water.
  - National Centre for Environmental Toxicology (NCET), WRc
  - National Poisons Information Services (NPIS)
- A list of contact names of experts/organisations in other related disciplines (e.g. epidemiologists, statisticians) who can advise on how to design an epidemiology study. Examples of such organisations include:
  - Communicable Disease Surveillance Centre (CDSC)
  - Medical Research Council (MRC)
  - Water Research Centre (WRc)
  - University departments of epidemiology and public health medicine
- Guidance on communication with the emergency services. In an incident, police, ambulance and fire should be well informed since the public may contact any one of these emergency services for advice.
- Information on how to link in with water sampling and chemical analyses. As the water company will be most appropriate to undertake the water sampling it is important to have established good communication links with local water

companies prior to an incident. Information on laboratories capable of carrying out chemical analysis should be included.

- In order for biological sampling to be of use this will need to be carried out as soon as possible in an incident. Ethical approval will be needed and so it will be important to detail exactly the procedures which need to be adhered to obtain approval. Detailed information will be needed on the procedures and the appropriate facilities to contact for obtaining biological samples.
- Although the choice of sampling frame will be dependent on the incident, it would be useful to ensure that suitable sampling frames are available in an easily accessible form. For example, in the case of water billing systems it is necessary to check that information is accessible in an appropriate form. If the sampling frame is to rely on GP registers, provisional ethical approval for the use of these systems should be obtained in advance so as to reduce delays.
- Outline structures for questionnaires should be included in the contingency plan and guidance on how large the sample sizes need to be to achieve the desired statistical power.
- Information should be included on contacts for printing companies and translators for other languages so as to consider ethnic minorities.
- Guidance on how to invoke a hotline, issuing public health messages and also how to involve the media.
- Preparedness to inform the local GPs who will receive enquiries about the study.
- Information on the experiences gained from other incidents is also important to share and could be included as background information to a contingency plan.

During an incident, the water company is invariably concentrating on detailed investigation of the source of contamination and the reasons for failure to detect and prevent it entering the water treatment works or distribution system. Furthermore depending on the incident, there may be other urgent pressures such as providing alternative water supplies to populations, issuing 'not to drink notices' and communicating with the media. Bearing these pressures in mind, it is not surprising that a water company would not be anticipating whether or not an epidemiological study will be initiated following the incident. Consequently, adequate water sampling for the purposes of estimating exposures for an epidemiological study may not be considered. This difficulty can only really be solved by making provision for resources to be available so that additional water sampling can be undertaken during the incident. The administrative and resource implications of this need to be resolved in advance of the incident taking place.

## 5. CONCLUSIONS

1. There have been only three epidemiological studies of incidents following acute chemical contamination of drinking water in the UK over the past twenty years. Although some incidents may go unstudied or completely undetected, the main reason why the studies have been so few is that the incidents themselves are rare.
2. Search of the English-language literature revealed some twenty studies, from which eleven were selected for detailed review. Selection was based on the size of the population at risk in the incident and on the availability and adequacy of published reports. This selection was therefore deliberately biased towards the larger incidents and better examples of epidemiological studies.
3. The review demonstrated that epidemiological studies of acute chemical contamination of drinking water are technically feasible. Nine of these eleven studies were successful in investigating and quantifying the effects of the contamination on the exposed population. Only three of the studies, however, could be said to add to basic scientific knowledge on the toxicology of the contaminant involved. These three studies involved small populations and were based on 'hard' toxic-endpoints.
4. The design of any epidemiological study will be dependent on the individual incident and the objectives which are being addressed. The review revealed two aspects of the studies that were critical for the quality of information that the studies were able to provide. They were:
  - the time interval between the onset of the incident and the start of the research
  - the provision of adequate information on the concentrations of the contaminant(s) in the drinking water to which members of the study population were exposed.
5. The review also drew attention to the importance of:
  - assessment of effects by means of hard end-points wherever possible
  - taking account of the possibility of psychological effects when people are aware that they may have been exposed to contaminated water;
  - making appropriate allowance for covariates such as age and pre-existing health status.
6. If it is desired that epidemiological studies be included in the response to future incidents, contingency planning is strongly recommended to provide guidance at an operational level. A number of guidelines have been suggested on what to consider

when planning for such studies and on what procedures to have in place. One of the key features identified for any contingency plan is to have already established good communication between all of the experts/organisations identified in the plan.

7. To ensure that appropriate water sampling takes place to support an epidemiological study, resources must be available in addition to those already committed to the investigation and management of the cause of the incident. As one aspect of this, further consideration needs to be given to the storage of perpetual rolling samples at water treatment works.
8. If epidemiological studies are to be technically successful it is extremely important that they take place in an ambience of public co-operation. This will be assisted by the promptness, openness and impartiality with which the study is presented, and by appropriate provision of public information throughout the incident as a whole.

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## GLOSSARY

### **Case-control study:**

Case-control studies are a form of epidemiological investigation to determine the strength of relationships between health effects and their possible causes. In the context of water quality studies case-control methodology involves gathering information about the exposure history of a group of 'cases', who have been diagnosed as exhibiting the specific outcome of interest, and comparing their exposure histories with those of a set of 'controls' who have not reported the condition.

This type of study is retrospective in the sense that membership of the groups is determined by the outcome, not by the exposure. The controls must be drawn from the same population as the cases, by a procedure that ensures comparability in terms of factors known to influence the defined outcome, but not ones directly linked to the potential hazard. [MacMahon and Pugh (1970)]

### **Chi-squared test ( $\chi^2$ ):**

In the field of statistical analysis there are a number of different procedures that involve a  $\chi^2$  test and a number of variations of the  $\chi^2$  test to meet different needs. In the context of the present report the  $\chi^2$  test is a method for analysing results presented in the form of a contingency table. The table may have just two rows and two columns (2 x 2) or may be more complicated than this. If the table is 2 x 2, the  $\chi^2$  test is an approximate alternative to the Fisher's exact test.

The objective of the test is to ascertain whether there is a connection between the basis of classification of the rows (e.g. exposure) and the basis of classification of the column (e.g. manifestation of symptom). [Bradford Hill (1977)]

### **Cohort study:**

Cohort studies constitute one important form of epidemiological investigation to determine the strength of relationships between health effects and their possible causes. The distinguishing features of cohort studies are:

1. The group or groups of persons to be studied (the cohorts) are defined in terms of characteristics that were manifest before the appearance of disease or effect under investigation.
2. The study groups so defined are observed over a period of time, or after an interval has elapsed, to determine the frequency or intensity of the effect. [MacMahon and Pugh (1970)]

**Contingency table:**

A contingency table is a way of presenting the results of an epidemiology study when both the exposure information and the health-effect information are presented in a categorical way. Usually the table shows the numbers of subjects (persons) cross-classified according to (a) whether or not they exhibited the symptom or effect of interest and (b) their level of exposure (e.g. high, medium, low).

**Fisher's exact test:**

A standard method for analysing results presented in the form of a 2 x 2 contingency table. If the table gives numbers of subjects cross classified by (a) whether or not they exhibited the symptom or effect and (b) whether or not they had been exposed, the outcome of the test indicates whether or not it is reasonable to believe that there is a connection between (a) and (b). The statistical calculations on which this decision is based are 'exact' in the sense that they do not involve any mathematical approximations. [Pearson and Hartley 1966].

**HAGCCI:**

Health Advisory Group on Chemical Contamination Incidents, DOH.

**Hard toxic endpoints:**

Symptoms of illness that are of an objective nature and are susceptible to clinical confirmation (e.g. methaemoglobinemia).

**Proportional risk:**

The proportional risk of exhibiting a specified symptom is the rate of occurrence of that symptom divided by the rate of occurrence of any one of a specified set of possible symptoms. [This proportional risk will in general be different for exposed and unexposed groups. The ratio of their respective proportional risks is the relative proportional risk]. [MacMahon and Pugh (1970)].

**Relative risk:**

The ratio of rate of occurrence of a specified illness amongst exposed persons, to the corresponding rate for unexposed persons. [MacMahon and Pugh (1970)].

**Soft toxic endpoints:**

Symptoms of illness that are of a subjective nature and cannot be confirmed by clinical investigation (e.g. headache, nausea).

## APPENDIX A RESULTS OF SEARCH

Table A.1. Epidemiological studies following acute chemical incidents

Country/Region	Year	Chemical	Population at risk	Source of information	Quality of report	Rev. a)	Ref. b)
Korea, Teagu City	1991	Phenol	2,000,000	Published paper	Adequate	Yes	1
UK, Dee	1984	Phenol	2,000,000	Published paper	Adequate	Yes	2
USSR, Ufa	1990	Phenol	600,000	Unpublished report	Adequate	Yes	3
UK, Worcester	1994	EDD	100,000	Published report	Adequate	Yes	4
UK, Lowermoor	1988	Aluminium sulphate	20,000	Published paper	Adequate	Yes	5
USA, Pittsburgh	1980	Chlordane	10,500	Published notes	Inadequate	No	12
USA, Michigan	1977	Fluoride	1,700	Published paper	Adequate	No	13
USA	1977	Developer fluid	>500	Published notes	Inadequate	No	14
USA, Alaska	1992	Fluoride	470	Published paper	Adequate	Yes	6
USA, North Dakota	1987	Ethylene glycol	400	Published notes	Inadequate	No	15
USA, North Carolina	1974	Fluoride	339	Published notes	Inadequate	No	16
USA, New Jersey	1992	Nitrite	312	Published paper	Adequate	Yes	7
USA, New Mexico	1978	Fluoride	265	Published paper	Adequate	Yes	8
USA, Georgia	1980	Sodium hydroxide	252 households	Published notes	Inadequate	No	17
USA, Connecticut	1986	Fluoride	127 households	Published paper	Adequate	No	18
USA, Tennessee	1976	Chlordane	105	Published paper	Adequate	Yes	9
USA, Vermont	1980	Fluoride	44	Published paper	Adequate	No	19
Canada, Ontario	1987	Nickel	43	Published paper	Adequate	Yes	11
USA, Wisconsin	1974	Phenol	26 households	Published paper	Adequate	Yes	10
USA, Various	1994	Copper	Unspecified	Published paper	Inadequate	No	20
USA, Vermont	1977	Copper	Unspecified	Published notes	Inadequate	No	21
USA, Ohio	1977	Carbon tet.	Unspecified	Published paper	Inadequate	No	22
USA, Georgia	1980	Phenol	Unspecified	Published notes	Inadequate	No	23
USA, Annapolis	1979	Fluoride	Unspecified	Published notes	Inadequate	No	24

Notes: a) Included in review b) see reference list p. 35-37. There are further examples of fluoride overdosing involving community supplies in the USA which have resulted in illness and which are not included within the table. This is because no published information was found for these studies.

## APPENDIX B      REVIEW OF INDIVIDUAL STUDIES

### B1      TEAGU CITY, KOREA, 1991

#### Source of information

Kim *et al* (1994)

#### Outline of incident

On 16 March 1991, 30 tons of phenol were accidentally discharged into the River Nakdong, 50 km upstream of Taegu City. The river is a major source of drinking water to Taegu and supplies about 2 million consumers.

The water authorities were unaware of the contamination until the water had reached consumers. Chlorination of the central water supply converted much of the phenol to chlorophenols which imparted a strong taste to the drinking water.

The paper mentions a second spillage of phenol into the river on 23 April but gives no further details of this. The paper does not describe any remedial measures following either incident. Monitoring for phenol in the central water supply after the first spillage continued only until 19 March.

Taegu City has two other sources of supply, the Kachang and Kongsan Lakes.

#### Objective of study

To assess whether there was an actual increase in the incidence of illness from the accidental spill of phenol and whether this increase was related to consumption of contaminated water.

#### Design of study

Study subjects were recruited from one class in each grade in each of 10 schools and comprised the school pupils together with their family members. The schools were randomly selected, six located in the contaminated area and four in the unexposed area.

The study subjects were divided into cohorts depending on their residential addresses, and further classified according to whether they thought they had been exposed to contaminated water. The 'true exposed group' denoted people who actually lived in the exposed area and who believed they were exposed. The 'false exposed group' denoted people who believed that they were exposed but who did not live in the exposed area. 'True' and 'false' unexposed groups were correspondingly defined.

Self-administered questionnaires were distributed through pupils on 24 and 25 May 1991, asking for information about 14 symptoms, 9 likely to be related and 5 unrelated to the contamination. The questionnaire also asked for demographic and medical information,

knowledge of the source of drinking water, and whether the respondent had noticed peculiar taste or odour in the tap water at the time of the incident.

At the time of the incident, phenol concentrations were measured in two reservoirs pumping from the Nakdong river. The paper mentions only a single determination of chlorophenol "in tap water", but it is unclear whether this was the only relevant determination.

#### Method of analysis and presentation

Symptom rates were presented for the true exposed and true unexposed groups and were compared by means of the  $\chi^2$  test. Symptom rates were also calculated for 'high', 'low' and 'unexposed' groups based on place of residence and water usage, and again compared by means of  $\chi^2$ . (The version of test used here is not explained).

#### Main findings

The study achieved a high response rate (82% of households) to its questionnaire. Information was returned from 6913 individuals of whom 5533 provided adequate information, 3089 in the true exposed group and 1444 in the true unexposed group.

The symptoms rates for the true exposed group were significantly higher than for the true unexposed group for each of the 'related' symptoms, except malaise. The rate was also significantly higher for 'fever' which had been declared as 'unrelated'. For the four other unrelated symptoms, rates were higher for the exposed group but not significantly so.

All of the 'related' symptoms showed gradients in going from 'high' exposure through 'low' exposure to 'unexposed'. This was also the case for two 'unrelated' symptoms, fever and tremor.

#### Authors' interpretation

The authors interpretation of the results is clearly that the increase in the incidence of symptoms was associated with exposure to the contaminated water. The authors claim that their analysis was based on 'true' exposed and unexposed cohorts to "rule out psychogenic effects".

#### Commentary

The authors correctly describe this study as a cohort study. In view of the method of selecting the subjects, the cohort cannot be regarded as randomly selected from the Taegu population. The method of recruitment could be described as 'cluster sampling' and is likely to give rise to correlations between the responses of individuals in the same family or recruited via the same school class. It is difficult to make allowance for such correlations at the analysis stage, and the authors have not tried to do so. The convenience and efficiency of this method of recruitment is therefore offset by some degree of statistical compromise, the importance of which is unknown.

One interesting feature of the study is the classification of respondents into 'true' and 'false' categories according to their own perception of their exposures. It is therefore disappointing that this classification was not fully exploited in the analysis. The numbers of false exposed (506) and false unexposed (450) subjects were large enough to enable an investigation of the 'psychogenic' hypothesis but such an investigation is not shown. It is not correct to assert that the analysis based on the 'true' categories "rules out" psychogenic effects: it simply combines them with the effects of other mechanisms. The authors' discussion of this could have been clearer. It correctly draws attention to the problem of exposure to water drunk away from home but this could perhaps explain the results for the 'false exposed' category, in which case their symptoms would not necessarily have been 'psychogenic' at all. The usage of the terms 'true' and 'false' needs more careful explanation in relation to the information on which the subjects were classified. The fact that many people (92%) in the exposed area noticed a peculiar smell or taste and would therefore have been aware of their exposure may well have influenced replies.

It is difficult to comment on the adequacy of the analytical data for concentrations of phenol and chlorophenol in the distributed water, because too little explanation is given. The authors indicated that the concentration of phenol in the tap water was 0.004 mg l<sup>-1</sup>. Such a level would not be expected to be associated with toxic effects due to phenol itself. The authors, however, did indicate that this was likely to be an underestimate of concentration since it was likely that the measurement was taken after the peak of the contamination had passed.

In general this study appears to have been well designed and executed, although the questionnaires were sent out rather a long while (2 months) after the incident. The study met its own objectives. It would have met the Department's main objective (i) and Objective (iv) but not (ii) which is mainly a result of the time delay. Its ability to contribute basic scientific information on the toxicology of the contaminants (Objective (iii)) was limited by the inadequacy of information about the mixture of contaminants to which the subjects were actually exposed.

## **B2 RIVER DEE, UK 1984**

### Source of information

Jarvis *et al* (1985)

Correspondence between Welsh Water, WRc and S.N. Jarvis

### Outline of incident

Water abstracted at several points from the River Dee is distributed to about two million consumers in north west England, including Liverpool and Chester, and north eastern Wales.

On about 25 January 1984 the River Dee became polluted with an unknown quantity of phenol and a much smaller amount of 2-ethyl-hexanol. This pollution was undetected before chlorination of the water during routine treatment converted much of the phenol to monochlorophenols, dichlorophenols and trichlorophenols which imparted a strong medicinal taste to the water.

Normal tests for taste and odour showed a "phenolic" taste in treated water on the evening of 25 January. The water suppliers altered their treatment practices and the treated water was thereafter satisfactory to these tests. It was believed that the band of pollution in the River Dee had passed. Polluted water had, however, entered the distribution system. The concentrations declined over the next three or four days, but were still detectable in some areas for up to one week.

During this time the public was advised that although the water was unpleasant it posed no important risk to health.

#### Objectives of study

1. To determine if there had been an increase in illness in the community during the time of the pollution incident.
2. To determine, if there was excess illness, whether it was associated with consumption of polluted water.
3. To determine, if there was excess illness, its impact on the health care system.
4. To determine the public health implications of the incident.

#### Design of study

The study comprised four separate epidemiological investigations:

1. Postal questionnaire to a random sample of households in each of three areas receiving different waters.
2. Examination of records of accident and emergency departments for the period 18 January - 8 February 1984.
3. An informal telephone survey to determine sickness absence among students of ten schools in North Clwyd.
4. A questionnaire to general practitioners requesting the number of surgery visits, home visits and patients with gastro-intestinal complaints (in the same areas as for investigation 1).

These studies took place only in the areas supplied by Welsh Water although water supplied by North West Water was also affected.

The published report was confined to the first of these studies and will receive most attention here. It appears that investigations 2-4 were not completed.

The three areas for this study were supplied by:

Service Reservoir A (Aston)	(initially believed to contain high concentrations of polluted Dee water) "high exposure area"
Service Reservoir B (Pen Brigog)	(pollution initially believed to have been more dilute than in A) "low exposure area"
Upland water	"unexposed area"

Postal questionnaires were sent to 250 quasi-randomly selected households in each area and information was requested from all members including:

- a) whether tap water was drunk during the incident;
- b) sources of water drunk outside the home;
- c) occurrence of seven specified symptoms during 26 January - 1 February.

The send-out time of the questionnaire is not given, but it could not have been before 6 February, 1984.

The study included no water sampling additional to that undertaken for operational purposes. Estimates of concentrations of phenol and chlorophenol based on available data were not very different between reservoirs A and B and so the questionnaire results for the two exposed areas were combined in the published tables.

#### Method of analysis and presentation

The rates of occurrence of symptoms were compared between the exposed and unexposed areas and the differences tested by means of  $\chi^2$  or Fisher's exact test. There appears to have been no standardisation for age. The problem of statistical dependence between the responses of members of the same household was recognised but regarded as unimportant.

Information about the dates of onset of symptoms (in exposed and unexposed groups) was presented on tabular form.

#### Main findings

The response rate for the questionnaire was 69% in the unexposed area and 72% and 77%, respectively, from Areas A and B.

During the incident the proportion of people who drank tap water was lower in the exposed area (71%) than in the unexposed (90%).

The proportion of respondents who reported any symptoms was significantly higher in the exposed area (33%) than in the unexposed area (9%). This finding was repeated for each of the specific symptoms. Restricting the analysis to subjects who had drunk tap water tended to sharpen the contrast. The excess of symptoms amongst the exposed group was not, however, confined to those who had reported bad tasting water. The presence of bad taste did not significantly increase the reporting of symptoms amongst the exposed group. However, the prevalence of bad taste was associated with an increase in the reporting of gastro-intestinal symptoms amongst the unexposed group.

#### Authors' interpretation

The data presented strongly support the hypothesis that consumers who drank the contaminated water developed illness, caused by one or other of the pollutants or by their mixture, although the estimated concentration of each of the components was below its previously reported toxic range.

#### Commentary

This is a competent study with appropriate statistical analysis and a well written report.

Two reservations about the sample selection: (1) that it may have taken place somewhat later than would have been ideal and (2) that individuals within the same household cannot be regarded as statistically independent, do not seriously detract from the study. Nor does the absence of age adjustment constitute a serious flaw, as symptoms rates seem not to have been strongly dependent on age.

The most serious drawback of this study does not fully emerge from the Lancet paper. The estimates of exposure were based on the results of only two samples of water from the distribution system (one from Service Reservoir A on 27 January and one from a domestic tap on 26 January served by the same treatment works but actually outside areas A and B). The concentrations presented in Table 1 of the Lancet paper involved extrapolation, over which there remains considerable uncertainty. Correspondence about this between the authors of the study and WRc, who carried out the analysis of these two water samples, continued until November 1986 without satisfactory resolution. The absence of satisfactory estimates of exposure considerably reduces the toxicological value of the study. In spite of the results of the analyses which took into account the ability of people to detect a taste or odour in the water, this study cannot eliminate the possibility that the effects may have been psychologically induced.

The study met the authors' objectives 1, 2 and 4. Their objective 3 would have been dealt with in the investigations 2 and 4, the results of which were not fully reported.

The study met the Department's Objectives (i), (ii) and (iv). It failed to meet Objective (iii) since the incident involved a mixture of contaminants, for none of which was the concentration adequately determined.

## **B3 UFA, BASHKIRIA, USSR, 1990**

### Source of information

For this incident our only source of written information is the Draft Interim Toxicology Report prepared for the World Health Organization (WHO) in May 1990. This is not the report of the results of an epidemiological study but a preliminary report on the incident including discussion of the design for an epidemiological study which the report recommends should be carried out. The report contains some information about case investigations of people reporting medical conditions that may be attributable to the incident. This information is not, however, presented in a way that could be regarded as a study. The following review therefore concentrates on the design of the proposed study. We have no information about whether the study was carried out.

### Outline of incident

The City of Ufa, with a population of about 1.2 million, has two water treatment works both using water from the River Ufa but abstracted at different points. The northern intake is upstream of the potential pollution from local industrial operations but the southern intake is vulnerable.

In March 1990, at the Khimprom factory, a large spill of phenol which should have been contained in a retention tank for surface drainage, escaped when melting snow caused the retention tank to overflow. The contents of the tank, with up to 100 cu metres of phenol, indirectly entered the River Ufa at a point between the northern and southern intakes for the Ufa drinking water supplies. This happened on or around 26/27 March.

From about 29/30 March the drinking water supplied from the southern system became seriously contaminated. The highest concentration of phenol measured was  $77 \mu\text{g l}^{-1}$  on 30 March. At this time there were complaints of taste and odour and a number of people (we are not told how many) reported illness possibly attributable to poisoning by phenol.

The report says that during the period when the contamination was worst, people were warned not to drink the water. We are not told whether alternative water was provided, nor for how long the warning remained in force, nor whether the advice was followed.

On 20 April 1990, WHO sought the help from the UK National Poisons Unit and from WRc to provide expert advice to the authorities in USSR on toxicological and analytical aspects of the incident and its investigation. This request was met by Dr H James (WRc) and Dr V Murray (National Poisons Unit) visiting Ufa to act as WHO Temporary Advisors. The visit took place on 1-4 May 1990 and resulted in the report previously cited. One of the aims of the report was to advise on the planning and execution of an epidemiological survey.

### Objectives of study

The objectives of the epidemiological survey would be:

1. to determine the proportion of the population exposed to phenols/chlorophenols;
2. to determine the illness attributable to such exposure;
3. to test the hypothesis that the illness was associated with water consumption; and
4. to determine whether there was a dose response relationship.

### Design of study

The report offers no discussion of the extent to which the available analytical data from samples taken from the distribution system at the time of the incident could be brought to bear on Objective 1. The design included no further sampling as this would have been pointless after a time lapse of several weeks.

The study is based on the estimation of symptom rates by application of a questionnaire to members of randomly selected households in three areas:

- South of Ufa
- North of Ufa
- 'Nearby uncontaminated' region

The choice of sampling frame was discussed but at the time the report was written it remained unresolved. No recommendation was made about sample size. It is suggested that "the administration of the questionnaire would probably need to be done by doctors ... rather than by postal distribution". The logistic implications of this were, however, not discussed, nor reflected in the draft questionnaire appended to the report.

The content of the questionnaire itself is discussed in the report and is set out in detail in a draft, based on that used in the Lowermoor incident (Study 5). The topics covered include:

- Detection of abnormal colour/taste/odour
- Water usage habits
- Changes in water usage habits following the incident
- Occurrence of symptoms (23)
- Absence from work/school
- Visits to doctor/polyclinic/hospital
- Pre-existing medical conditions

### Method of analysis and presentation

Not specified.

### Main findings and authors' interpretation

It is not known whether the survey has been carried out.

### Commentary

Any comments on this report need to be moderated by the recognition that it was described as a 'preliminary draft' and had been put together in a very short interval of time. The report contains some useful discussion applicable to studies of pollution incidents in general. It does, however, also include some confusing statements, particularly in the description of the design. Furthermore some questions on vital aspects of the design appeared, at the time that the report was written, to have still been unresolved.

The recommended design is clearly for a cohort study comparing the rates of occurrence of symptoms amongst the populations of three geographical areas. The discussion of the design on pages 14-16 does however include terminology which is more appropriate to case-control methodology. This tends to undermine confidence in the report since case-control methodology - a quite different type of study - is not being recommended.

However quickly the study might have been carried out, there would have been an inevitable delay between the incident and the study, since over a month had already elapsed by the time that this report was produced.

It is impossible to comment fully on the method of recruitment of subjects, because it is not specified. The structure of the questionnaires appears to be aimed at the recruitment of families, but this does not fit easily with the suggestion that the interviews would be conducted by trained medical personnel. It is not clear whether this would be achieved by the interviewer visiting the family home (expensive) or by arranging for the family all to be interviewed at a central point such as a clinic (difficult to organise). If the latter there would appear to be no advantage in recruiting families rather than individuals unless it were to ensure representation of all age-groups. The main comment on these aspects of design is that they had not been well enough thought-out.

The questionnaire itself does appear to have been carefully designed. The questions about timing of when people noticed abnormal water, or noticed the onset of symptoms are, however, rather ambitious in the level of detail that subjects were expected to recall. This would have been more of a problem the longer the delay before the study was actually carried out.

It is not clear from the report how much information was available about the concentrations of phenol and its by-products in the distribution system at the time of the incident. It is therefore impossible to comment on the success of the design from this point of view.

Subject to the removal of uncertainties and reservations mentioned above, the recommended study would be capable of meeting its own objectives and the hypothetical objectives set by the Department, apart from Objective (ii) which would not have been

met because of the time delay. It would be interesting to know how far these objectives were achieved in practice.

## **B4 WORCESTER, UK, 1994**

### Source of information

The Report of the Department of Public Health Medicine by Fowle *et al* (1994), which is also to appear in the *Journal of Epidemiology and Community Health*, 1996, **50**(1).

### Outline of incident

From around 8 am on Friday 15 April 1994, two little-known solvents 2-ethyl-4-methyl-1,3-dioxolane (EMD) and 2-ethyl-5,5,-dimethyl-1,3-dioxane (EDD) were present in water distributed from the Barbourne treatment works where water is abstracted directly from the River Severn. The Barbourne works serves a population of about 100,000 people in Worcester and nearby areas. From 12.25 p.m. people in Worcester were told not to drink the water and this warning was spread to other affected areas in the afternoon and evening. On the basis of toxicological advice, people were told that they could drink the water again at 5.15 p.m. on Saturday 16 April. The concentrations of EMD and EDD were also reduced approximately 10-fold by the use of powdered active charcoal at Barbourne from 6 p.m. on 16 April. However, the water continued to smell at various points in the distribution system for up to a week.

The nearby town of Evesham (population 15, 000) was initially thought to be affected but this later proved not to be the case.

Approximately 3,500 phone calls were received on the Health Emergency help line over the weekend of the incident. 86 of these calls reported illness.

### Objectives of study

1. To establish any true increase of illness associated with exposure to the contaminated water.
2. To assess the extent of association between noticing the water had an unusual smell or taste and exposure to the contaminated water.

### Design of study

The study is based on a comparison of disease incidence rates, as estimated by survey, in three areas:

- Worcester (“study area”)
- Evesham (control area 1, where people may have thought that their water was affected)

- Droitwich (control area 2, from a separate borehole supply)

1000 private households were selected in each area “using a combination of systematic and random methods”. In each household all members were invited to complete separate questionnaires or to have questionnaires completed for them.

The questionnaires asked for indication of the occurrence of 14 symptoms on 15, 16 or 17 April and asked for detailed information on water usage and on the detection of smell, separately on each of these days. The questionnaires were sent out on 22 April.

The study included no water sampling additional to that undertaken for operational purposes.

#### Method of analysis and presentation

The results of the survey were analysed by means of contingency tables in which the number of occurrences of symptoms were broken down into categories representing:

- area
- water consumption, quantified in terms of ‘cups’.
- whether or not “smell” had been detected

$\chi^2$  tests were applied to test hypotheses concerning systematic differences in rates. The methods of comparison included allowance for age and sex.

#### Main findings

The response rate of households to the survey was 65% in the “study” area and 56% and 57% in the control areas. 3861 individual questionnaires were returned from the 1774 responding households.

The prevalence of one or more symptoms was higher in the “study area” (17%) than in the control areas (7%) and the difference between rates was significant for 10 of the specific symptoms when considered separately. The differences were highly significant ( $p < 0.001$ ) for diarrhoea, nausea, headache, stomach pains, skin irritation and sore throat.

The excess prevalence in the “study” area was shown to be specific to those who had drunk mains water and it showed a gradient with the quantity of water consumed. The excess prevalence, however, also appeared to be confined to those who had noticed that the water was “smelly”. For those who had not noticed, the rate of symptoms was not different from that reported by controls, and did not show a convincing gradient with the quantity consumed.

#### Authors’ interpretation

The authors’ interpretation of these findings is that the reporting of symptoms was associated with noticing the contamination not with the contamination itself. The possibility that the excess could be due to differences in response rates between the three

groups is discussed but rejected as “unlikely”. The authors’ interpretation rests in the assumption that the concentrations of the contaminants were uniform throughout the study area and that the respondents ability to smell the water was not a manifestation of spatial or temporal variability in the concentration itself. The authors therefore tend to attribute the higher rates of reported symptoms to the customers ability to detect an unusual taste or smell, rather than to a toxic effect of the compounds themselves.

### Commentary

This is a competent, lucidly reported and extremely interesting study. The strong points are that it took place rapidly (questionnaires were sent out just one week after the incident started), that it included two control groups, achieved adequate sample sizes and that the statistical analyses are sound. Also, from a toxicological viewpoint, the symptoms for which information was obtained were of sound choice.

From a technical point of view there are three reservations about the design and execution of this work.

- a) Rather low response rates and uneven response rates between the groups make for difficulty with interpretation. Low response rates may, however, be inevitable if the survey is conducted by post.
- b) In the statistical analysis it appears that the responses of members of the same household were assumed to be statistically independent. This assumption is doubtful, especially in view of the authors’ psychological interpretation of the results.
- c) The absence of analytical data on the variability of EMD and EDD within the study area opens a major loophole in the authors’ interpretation and weakens the conclusions that can be drawn from this work. Although the authors recognise this and bring good reasons to support their view, it remains a point of difficulty.

It can be said that this study met its own first objective but failed to meet its second, since no concrete evidence is given for the assumption that consumers who failed to detect smell were actually exposed to the same concentration as those who had. This deficiency could have been met only by a more extensive programme of sampling at the time when the incident was taking place.

With regard to the Department’s objectives the study not only met the primary objective but also Objectives (ii) and (iv). In view of the uncertainty in interpretation, the study cannot claim to have added much to our understanding of the toxicity of the contaminants. It has however, highlighted the importance of consumers’ anxiety and its potential to confuse the conclusions of a study based on self-reporting of rather ‘soft’ toxic endpoints (e.g. headache, nausea).

## **B5 LOWERMOOR, NORTH CORNWALL, UK, 1988**

### Source of information

Rowland *et al* (1990)

### Outline of incident

On 6 July 1988 a relief driver for a chemical company delivered 20 tons of aluminium sulphate solution to the Lowermoor water treatment plant. Unfamiliar with the layout of the works, which was unmanned, he poured the aluminium sulphate solution into the disinfection contact tank, from which it was distributed in the mains supply. The mistake was not discovered until several days had elapsed, during which some 20,000 consumers had received excessive concentrations of aluminium sulphate in their drinking water.

Because of the cause of the incident, the chemical involved and the way the public became aware of it, there was considerable critical attention in the media and anxiety in the local community. This led on to calls not only for technical investigation but also for litigation and redress. 'Studies' were instigated not only by the medical authorities but also by other interested parties.

The present review is concerned only with the official epidemiological survey reported by Rowland *et al*.

### Objective of study

The objective of this study was to describe and quantify the acute symptoms attributed to the incident.

### Design of study

This was a cohort study, comparing the incidence of symptoms in the exposed population (supplied by Lowermoor) with the incidence of symptoms in a nearby control area (Bastreet) where the water had not been affected. The study sample comprised the members of 500 households in each supply area, randomly chosen from the lists used for water rating.

A two-part questionnaire was mailed to each household. The first part, addressed to the head of household, asked for demographic information and questions about whether abnormal water had been observed. The second part, a copy of which was to be completed by each individual, contained questions about:

- residence in the district at the time of the incident
- the consumption of mains water before and after the incident
- the occurrence of each of 19 specific symptoms
- visits to the doctor or hospital
- time off school or work

- evidence of prior or chronic illness

The study included no water sampling beyond that which had already been carried out. This appears to be satisfactory and additional sampling would not have been appropriate as the study was not designed until after 15 August, over a month after the incident had taken place. The questionnaires were not sent out until early November, an interval of some four months after the incident.

The study provided no on-going monitoring of long-term effects as these were being investigated in other work.

#### Method of analysis and presentation

The results of the study include information about response rates and the demographic details of the respondents. The principal method of analysing the results was by presenting the numbers and percentages of respondents reporting each symptom, and comparing the percentages between the two groups (exposed, control). The results of these comparisons were presented as ratios (i.e. relative risks), for which 95% confidence intervals were reported, although the method of deriving these intervals was not described.

The incidence of symptoms was also analysed in terms of proportional morbidity rates and reported in terms of relative proportional risks. 95 percent confidence intervals were given for these relative risks but the method of deriving these intervals is not described. The analyses were repeated after exclusion of respondents who had shown evidence of a "long-standing illness", and again after exclusion of subjects over 65 years of age. It is not completely clear whether the corresponding analyses were also repeated in terms of relative risk.

The relationship between water consumption and symptom rates were explored by exhibiting, for each symptom, the relationship between daily water consumption (3 levels) and the symptom specific relative proportional risk.

#### Main findings

The response rate to the questionnaire was rather low, 45% of households, but with not much difference between the groups. The demographic features of the two groups were similar, although there were some significant differences, with respondents in the exposed area tending to be older.

The usual water consumption of the respondents (before the incident) showed some differences between groups but the categorical presentation of the data did not provide a clear indication of whether the consumption in one group was generally higher than the other. However, about half of the respondents in the exposed group reported that they had changed their water consumption at some time in July, compared with only 2.4 % in the control area.

A much higher proportion of households (67%) in the exposed area noticed abnormalities in their water than in the control area (17%).

Half (49%) of the respondents of the exposed area reported that they had experienced unusual symptoms since the start of July 1988, compared with 10% in the control group. The rates of reporting all of the 19 individual symptoms were elevated for the exposed group over the control group and the relative risks were significantly greater than 1 (Table 7).

The analysis of proportional morbidity “to determine whether particular symptoms were more likely to occur in symptomatic respondents from the exposed group than ... in the control group” (p.170) revealed 3 symptoms whose rates differed significantly between the two groups. Painful joints were more likely to be reported by symptomatic individuals from the exposed area, while ‘fever’ and ‘shivers’ were more likely to be reported by symptomatic individuals from the control area.

A higher proportion of subjects in the exposed area reported that they saw their doctor regularly for ‘long-standing illness’ and that they had been on prescribed medicine before July 1988. Exclusion of the respondents who had shown evidence of long-standing illness did not remove the significance of joint pains (nor of ‘fever’ and ‘shivers’) when the analysis was conducted in terms of relative proportional morbidity. The wording of the last sentence on p.170 could be construed as meaning that the exclusion of these respondents from the analysis in terms of relative risks rendered the differences previously reported in Table 7 as no longer significant.

#### Authors’ interpretation

The authors reveal that in August 1988 the local Medical Officer of Environmental Health had written a letter to all residents of the exposed area and that most of the symptoms included in the questionnaire had been mentioned as a possibility in that letter. The existence of this letter must be taken into account in interpreting the results of the study and (we surmise) would have been the main reason for analysing the results of the study in terms of proportional morbidity.

The authors interpret the excess proportional morbidity for joint symptoms as a genuine effect of exposure to the contaminated water or to the anxiety that accompanied such exposure. The authors did not make the corresponding interpretation of the reduction in proportional morbidity for ‘fever’ and ‘shivers’, although the supporting results were of equal weight to those for painful joints. This reduction in proportional morbidity for fever and shivers may simply indicate that most of the other symptoms were increased by exposure.

The authors drew attention to the faulty perception of water quality by a number of respondents who reported changes in water quality in the control area or changes in the exposed area that were inconsistent with the date of the incident.

## Commentary

This is an interesting paper but the study contains such serious weaknesses as to prevent meaningful conclusion other than that the results give powerful evidence for the existence and importance of psychological effects.

The study took place much too long after the event. The intense interest by the media, the extent of public anxiety and the letter from the MOEH would have made it virtually impossible to conduct a successful study of 'soft' endpoints amongst people who were aware of their exposure status. It might be even be said that the MOEH's letter undermined the validity of the research.

The study was based on a completely satisfactory definition of the exposed and unexposed groups, an appropriate method of recruitment and a well designed questionnaire. Furthermore the analysis included adjustment for pre-existing health status of the respondents. These strengths cannot, however, eliminate the possible biases attributable to psychological factors or to the worryingly low response rate.

The use of proportional morbidity as the method for comparing the exposed and control groups was a reasonable approach to assessing whether the excesses of specific symptoms amongst the exposed group were attributable to the exposure rather than to a general psychological effect. The interpretation of the results from the analysis (Table 8) does, however, really need to allow for the multiplicity of hypotheses being tested. The declaration of one significant effect out of a possible 18 is not surprising when the test was carried out at the 5% level. This result would have been noteworthy only if 'painful joints' had been declared in advance as the specific hypothesis of interest. The same comments apply to 'fever' and 'shivers', although the authors chose not to interpret the negative associations of those symptoms with membership of the exposed group.

This study was able to meet its own objectives only to a limited degree. The study described and quantified the acute symptoms reported by members of the two groups (exposed, control) but was unable to make a convincing attribution of those symptoms to the possible toxic effects of the water. This study would therefore have failed to meet the Department's main objective and Objectives (ii) and (iii). The study does however, shed oblique light on the management of the incident and some lessons can be learnt on this from reading between the lines.

## **B6 ALASKA, USA, 1992**

### Source of information

Gessner *et al* (1994)

### Outline of incident

On May 21 1992 in Hooper Bay, Alaska, a water supply which served approximately half of the population of the village was overdosed with fluoride (termed 'Water System 1'). On May 23 it was noted by the local clinic that there an increase in the number of residents who had become ill shortly after drinking water from Water System 1 and it was turned off. The outbreak resulted in a number of residents becoming ill, one serious illness and one death.

The Water System 1 supplied water to 470 people as opposed to Water System 2 which supplied 375 people. These systems comprised wells and holding tanks from which people collected their water, without distribution pipework to individual homes.

High concentrations of fluoride had been previously reported in Water System 1 but because of misunderstanding and human error the appropriate actions had not been taken.

### Objective of study

The objective of the study was not explicitly stated but was obviously to describe and quantify the effects of the incident on the population.

### Design of study

The epidemiological investigations comprised three studies:

- a) A case-control study based on patients first seen at the local clinic on May 21, 22, 23 or 27 and interviewed there on 27 May.
- b) A cohort study based on the members of 15 households in the part of the village served by Water System 1, and 17 households served by Water System 2.
- c) Biochemical measurements on a sub-sample of the subjects recruited in (a) and (b).

For the purposes of statistical analysis these three studies were considered separately. Four individuals appeared in both studies (a) and (b). It would appear that the same questionnaire was applied in both studies.

#### (a) Case-control study

Cases were defined as residents who attended the health clinic on May 21-23 and who had at least one of the following symptoms compatible with fluoride poisoning: nausea, vomiting, diarrhoea, abdominal pain, or numbness or tingling of the face or the

extremities. These cases were then asked to visit the clinic on May 27 with any available family members. These individuals, as well as patients being seen at the clinic for any other reason on May 27, were interviewed and responded to a questionnaire that included questions about symptoms and water consumption. The asymptomatic respondents interviewed on 27 May were designated as controls.

#### (b) Cohort study

On May 28, a household survey was conducted by random selection of 15 adjacent households supplied by Water System 1 and 17 adjacent households served by Water System 2. Information was collected on all residents of each household and also about those not at home and included questions about symptoms and water consumption.

#### (c) Biochemical measurements

The recruitment of subjects to the case-control study and cohort study was followed by biochemical measurements on subsets of cases and controls on May 27 and 28. The methods of selection of these subjects were not described but they appear to have been taken from the pooled membership of the previous studies. Blood and urine specimens were collected from 20 case patients and blood or urine alone from another 7 cases. Urine specimens were also collected from 15 control subjects, 3 of whom also provided a blood sample.

Water samples were collected from the two water systems and from residents who still had water from System 1 in their home.

#### Method of analysis and presentation

The results of the case-control study were presented in terms of the odds ratios associated with (1) living in the area served by Water System 1, (2) drinking water from System 1 and (3) drinking water obtained from System 1 on May 21, 22 or 23.

The results of the cohort study are presented simply as comparisons between attack rates between the residents of Section 1 and Section 2 and between subsets of the residents of Section 1 defined in terms of their water consumption.

The results of the biochemical follow up were presented in terms of descriptive statistics (medians and correlation coefficients).

#### Main findings

The results of the case-control analysis gave overwhelming evidence that the risk of being a case was strongly influenced by factors (1), (2), (3) (Table 2).

The cohort study (Table 3) revealed an attack rate of 63% amongst Section 1 residents, of 71% amongst Section 1 residents who usually drank from System 1, and 91% for those who drank from System 1 on May 21, 22 or 23.

The biochemical measurements indicated higher median urinary and serum fluoride concentrations in the cases than in the controls. Also, the serum fluoride concentrations in case patients correlated strongly with the duration of the illness. In case patients there was biochemical evidence of disordered mineral homeostasis (magnesium, phosphorus) and cellular damage (e.g. lactate dehydrogenase). The estimated fluoride dose also strongly correlated with urinary and serum fluoride concentrations.

#### Authors' interpretation

It was very clear both from the epidemiological results and the biochemical follow-up that the illness was attributable to fluoride poisoning. The authors discuss the toxicological aspects of their findings and analysed the likely causes of overdosing in the water treatment plant.

#### Commentary

The effects of this incident were so strong and involved such a high proportion of the exposed population that almost any epidemiological method would have been capable of revealing them. The dual approach (case-control and cohort studies) taken in this work was quite satisfactory, although the presentation of the methodology is slightly confusing. Strong points for these studies were that they began quickly following the incident and that the analytical data for the water samples were adequate since no distribution system was involved. The method of recruiting households to the cohort study was not very satisfactory; the choice of a random starting point would be enough to ensure that the sample is random, but not to ensure independence between subjects. Independence as well as randomness of subjects is, however, an assumption underlying the analysis in Table 3.

Since the objective was not formally stated it is not possible to say whether it was achieved. The study would, however, have met all of the objectives set out by the Department. This was an incident that could and should have been avoided and the study carries powerful messages about the prevention of any similar combination of events in the future.

## **B7 NEW JERSEY, USA, 1992**

#### Source of information

Askew *et al* (1994)

#### Outline of incident

On October 20, 1992 more than 40 children from one elementary school visited the school nurse following onset of blue lips and hands, vomiting and headache within a 45 minute interval during and after the school lunch period. Forty-nine children were seen by

doctors that day and laboratory analysis revealed methaemoglobinaemia in many of the children; 14 were hospitalised although all recovered within 36 hours.

### Objective of study

To determine the cause of the incident.

### Design of study

A case-control study was undertaken supplemented by environmental and laboratory investigations.

The population under study consisted of all 312 students enrolled in the school. Local hospitals were contacted by telephone to determine if there were any visits by the children from the school. Cases were selected based on the laboratory diagnosis of methaemoglobinaemia (methaemoglobin levels >2%), which resulted in 29 students. The twenty children whose methaemoglobin levels were missing or were <2% were excluded from analysis. Controls were obtained by selecting every third name from school roster. The parents of the 29 students who met the case definition and 52 (of 88) controls were interviewed by telephone within 30 hours of the onset of illness. The information obtained included child's weight, lunch period, food consumption history for the day in question, symptoms, place of onset of symptoms, physician or hospital contact and whether a methaemoglobin level was obtained.

Samples of all foods served on October 20 were obtained as well as samples from the potable water system, boiler system and boiler treatment solution for chemical analysis.

### Method of analysis and presentation

The factors that might have been associated with an increase in the risk of methaemoglobinaemia were all treated as binary attributes. For each factor, the odds ratio for methaemoglobinaemia was calculated. Confidence intervals for these odds ratios were calculated by modern non-parametric methods (StatXact).

### Main findings

There was no significant difference between cases and controls in terms of sex or age. Of the 29 cases, methaemoglobin levels ranged from 3 to 83%. 14 individuals had methaemoglobin levels above 20% which is associated with moderate to severe poisoning. Following interview, it was found that all 29 cases and 33% of the controls ate soup during the school lunch. Also, the odds of being a case was 4.8 times greater for individuals who had more than one serving than for those only having one serving. No other lunch food item was independently associated with illness.

On the day of the outbreak, soup had been diluted with water from the kitchen using both the hot and cold water taps. Laboratory investigation of the left over soup served at lunch showed abnormally high concentrations of nitrite ( $459 \text{ mg l}^{-1}$ ) and the presence of sodium metaborate. These substances were major components of the boiler treatment solution. In comparison undiluted soup from the same lot had only  $2 \text{ mg l}^{-1}$  of nitrite. Detectable levels of nitrite were found in samples taken from the school's domestic hot water system taken on the same day. It was also found that the nitrite level in the boiler was  $11 \text{ mg l}^{-1}$  whereas in a properly conditioned boiler it should be 300 to  $500 \text{ mg l}^{-1}$ .

The symptoms which were commonly reported by the cases (cyanosis, nausea, abdominal pain, vomiting, dizziness and burning mouth) were compatible with nitrite poisoning and the prevalence of these symptoms was much higher in cases compared to controls.

#### Authors' interpretation

The cause of methaemoglobinaemia was determined to be nitrite poisoning. This was traced to soup which had been contaminated via dilution with water taken from the domestic hot water system which was contaminated with nitrite. Direct introduction of boiler additive into the hot water coil tap during the boiler's conditioning emerged as the probable cause of contamination.

#### Commentary

This study is a competent one and has a number of strong points. The study took place rapidly (30 hours) and food and water samples were collected on the day of the incident for analysis. The selection of cases was good which was to some extent aided by the toxic end-points which were observed. Cyanosis (blue lips and hands) cannot be psychologically induced but can be quantified on the basis of laboratory investigations of methaemoglobin levels. The authors made good use of this and selected cases only on the basis of laboratory confirmation of methaemoglobinaemia rather than on symptoms alone. Controls were also selected quasi-randomly in an appropriate way.

Although the detailed questionnaire was not given in the paper, since the illness occurred rapidly following the lunch period, it appeared to have concentrated on food consumption history for the day. Since illness was associated with the consumption of diluted soup it was fortunate that the environmental analysis had also included samples from the potable water system, boiler system and boiler treatment solution.

The authors met their own objective in discovering the cause of the outbreak of the illness. In satisfying the Department's objectives it can be said that the study met Objectives (i), (ii), and (iv). It also cannot be said to add anything new on the toxicology of nitrite and therefore failed to meet Objective (iii). This may have been met if more detailed information had been given on estimates of doses which were associated with symptoms.

## **B8 NEW MEXICO, USA, 1978**

### Source of information

Hoffman *et al* (1980)

### Outline of incident

On November 17 1978, fifteen children were sent home from an elementary school by the school nurse because of the acute onset of gastrointestinal symptoms. Several of the students commented that the water tasted bitter and salty and so it was immediately assumed by staff that the water was the responsible agent. A message was quickly disseminated not to drink the water and the Epidemiology Unit of the Health Services Division were contacted who immediately initiated an investigation.

### Objective of study

The authors do not explicitly state their own objectives but it would appear that they were to define the nature and cause of illness which was strongly suspected to be related to water consumption.

### Design of study

A telephone survey of all of the 246 students and 19 staff was conducted. A standard message was read to the parent of each child informing them of the incident and a questionnaire was administered either directly to the school children or to their parents. Children's statements were confirmed by their parents. Approximately 75% of the 265 population was contacted and interviewed by 11.00 p.m. on the day of the incident.

From the information obtained in the surveys, a case was defined as illness in a person meeting the following criteria

- a) The person attended the school on November 17.
- b) The person had the onset of symptoms after 8.45 am on November 17.
- c) The symptoms included at least one of the following: nausea, vomiting or abdominal pain
- d) The person did not have fever.

To determine the duration of symptoms, a follow-up survey of the ill persons was conducted one week after the incident. Also, school records for the two weeks before the outbreak were checked to determine the usual number of children who left school each day because of illness.

### Method of analysis and presentation

The association of illness and the consumption of drinking water at school was analysed by chi-squared analysis. A contingency table was presented showing the break-down of numbers of ill persons by school grade.

### Main findings

Analysis of records of absence for the two weeks preceding the incident revealed an average 6 students per week (1.5 students/day). Therefore 15 ill students in a single day represented a marked increase above the base line of absence.

In all, 207 persons were interviewed (78.1%) and 34 of these met the case definition (attack rate 16.4%). Of the 207 people interviewed, the drinking water habits were ascertained for 148 persons and the association between illness and consumption of drinking water at school was significant.

Of the 34 cases, the most common symptoms in the outbreak were abdominal pain (79%), nausea (68%) and vomiting (32%) and 21% of the cases reported all three symptoms. Less common symptoms included weakness, diarrhoea and muscle twitching and excess salivation. None of the cases reported systemic effects of fluoride poisoning such as muscle spasms, tetany, convulsions or shock. All patients became ill within two hours after the first possible exposure and based on the follow-up study symptoms were generally of short duration and recovery was within 24 hours.

Water samples obtained from the drinking water fountains in the hallway of both school buildings on the day of the incident found fluoride concentrations to be extremely high at 375 and 93.5 mg l<sup>-1</sup>. Investigation of the fluoridator revealed that it had been faulty.

Based on water consumption information, estimates of the ingested doses of fluoride ranged from 1.4 mg to 90 mg.

### Authors' interpretation

The authors concluded that the outbreak of illness was due to acute fluoride poisoning as a result of drinking contaminated water. The symptoms of all patients were mild and generally of short duration, which the authors considered consistent with the ingested doses of fluoride.

### Commentary

The strong points of this study was that it was undertaken rapidly and that, because of the small population at risk, the majority of individuals were able to be interviewed. This meant there was unlikely to be bias in the recruitment of subjects. The study contained no unexposed group but the 'base-line' rate of absence from school was established from the records from before the incident took place.

The detailed questionnaire was not given in the paper and so it is difficult to comment on the objectivity of the assessment of toxic effects. However, the criteria (b), (c) and (d)

chosen to define a case were simple and appeared sensible. (Criterion (a) should not have been a condition for being designated a case, but for inclusion in the study).

Water samples were rapidly analysed on the morning of the incident and this provided a relatively good basis on which to estimate individual exposures. From information on water consumption, estimates of the ingested doses of fluoride ranged from 1.4 mg to 90 mg which the authors considered consistent with mild symptoms and relatively short duration of illness. The authors, however, calculated these doses in a rather simplistic manner and although the higher dose is expected to cause such symptoms, a dose of 1.4 mg is highly unlikely to result in such toxicity. This finding highlights the difficulty in estimating doses associated with acute toxicity and this problem has occurred in a number of incidents of fluoride overdosing.

The study did not attempt to investigate the relationship between attack rate and the estimated dose except in as far as the latter was dependent on the school building (A or B) in which the class was accommodated.

It appears that the study met its authors objectives and DWI objectives (i), (ii) and (iv). It did not contribute anything new on the toxicology of fluoride (Objective iii).

## **B9 CHATTANOOGA, TENNESSEE, USA 1976**

### Source of information

Harrington *et al* (1978)

### Outline of incident

At approximately 5.00 p.m. on March 24 1976, a resident of Chattanooga noted that his tap water turned milky and smelled like insecticide spray. The water company was notified and further reports of a similar nature were recorded from other residents of the area during that evening. The contaminant was identified as chlordane and the water company promptly turned off supply to the 42 affected houses. The number of persons living in the affected houses was 105 and the cause of the incident was determined to be back siphonage.

### Objective of study

The objective of the study was not explicitly stated by the authors but it would appear that it was to determine the extent of exposure to chlordane and the nature of any illness related to this exposure.

### Design of study

The study was based on a door-to door health survey conducted on March 26 and 27, and included all 105 persons living in the affected houses. The residents were asked about the occurrence of symptoms which could be associated with exposure to chlordane and which they might have experienced during the 48 hours following the incident. Although the authors did not specifically list the symptoms for which information was obtained, it appeared that these centred on gastrointestinal and neurological symptoms. The water exposure history was also acquired during the interview and 71 of the 105 people gave a history of contact with contaminated water through drinking, bathing or cooking. A serum sample was obtained from these 71 persons in order to further evaluate the extent of exposure to chlordane by measuring serum chlordane metabolite residues.

Between March 25 and 27, water samples were obtained from the 42 affected houses in the area and chlordane concentrations were determined. These ranged from <0.1 to 92,500  $\mu\text{g l}^{-1}$ .

Two months later, repeat serum samples were obtained from 11 of the 13 symptomatic residents.

### Method of analysis and presentation

The paper gives no formal analysis of symptom rates in relation to exposure.

For those individuals who had contact with water, descriptive statistics (geometric mean, 95% confidence limits) were used to assess whether the serum levels of chlordane metabolites of symptomatic individuals were different from the 58 non-symptomatic individuals.

### Main findings

Of the 71 residents who had contact with contaminated water, 13 (18%) experienced symptoms compatible with chlordane exposure. Four complained of gastrointestinal symptoms (nausea, vomiting or abdominal pain) and neurological symptoms (dizziness, blurred vision, irritability, headache, parasthesia, or muscle dysfunction). Nine others had gastrointestinal symptoms alone or isolated neurological symptoms. All residents who denied contact with contaminated water were symptom free.

Serum analysis indicated that levels of chlordane metabolites (transnonachlor, oxychlordane) were not significantly different between the 58 non-symptomatic and 13 symptomatic individuals at the time of the incident. However, there was a significant rise in serum oxychlordane levels in symptomatic individuals when tested 2 months later.

### Authors' interpretation

The authors' interpretation of their findings was that of the 71 residents exposed, 13 had symptoms or signs compatible with mild acute chlordane toxicity. Although serum levels of chlordane metabolites measured shortly after the incident did not correlate with the recorded symptomatology, re-testing of the symptomatic residents 2 months later

revealed a possible rise in oxychlordan levels which the authors interpreted as being supportive evidence that an acute exposure had occurred.

### Commentary

This study design has a number of strong points:

- a) It took place rapidly (interviews were carried out within 2 days).
- b) The small population involved enabled the whole population potentially at risk to be included in the study.
- c) Water sampling was carried out for all the affected houses very quickly enabling a good estimate of an individual's exposure.
- d) Serum analysis of non-symptomatic and symptomatic exposed persons was undertaken to try to confirm the link between exposure and symptoms.

The main comment on the study is that in view of the very detailed information which was obtained, additional toxicological findings could have been published. For example, estimates of the doses which were associated with symptoms of chlordan toxicity and more details on the actual symptoms reported with an individual's exposure would have been useful. The results from the serum analysis which were carried out during the time of the incident were surprising in that the mean serum levels of chlordan metabolites were lower in the symptomatic individuals than in the non-symptomatic individuals. However, the 95% upper confidence limit was much higher for the symptomatic individuals indicating that this may have been a chance finding. A more detailed breakdown of the serum analysis results would have been helpful in the interpretation of the data.

In the follow-up study, serum analysis for chlordan metabolites indicated a significant increase in the levels which suggests that acute exposure had occurred. However, it would have been useful to also include a small sample of non-symptomatic people who had been exposed and compare these results with those from the symptomatic individuals. If a difference in metabolite levels had been seen, this would have added more weight to the interpretation that symptomatic individuals had been exposed.

Since the objective of the study was not formally stated it is not possible to say whether it was achieved. The study, however, would have met the Department's primary Objective (i) and Objectives (ii) and (iv). However, in view of the lack of toxicological details and dose estimates reported, it cannot be said that to have added much to our understanding of the toxicity of the contaminant.

## **B10 WISCONSIN, USA 1974**

### Source of information

Baker *et al* (1978)

### Outline of incident

In July 1974 the derailment of a freight train resulted in the spillage of 37,900 litres of phenol in a rural area near to the town of East Troy, Wisconsin. A large amount of the spilled phenol was recovered but not enough to prevent contamination of groundwater supplying wells for nearby houses.

Most families continued to drink their well water for several weeks after the spill until an unusual taste or odour was noticed. Thereafter they obtained their water from alternative sources. In mid-November the spill site was flushed with water in an attempt to remove the contamination of phenol in local wells but this was unsuccessful. The contamination seemed likely to persist for many years and so the wells were closed permanently and a new water supply system was constructed.

There were 26 houses in the neighbourhood of the spill but they were not equally affected.

### Comment

This incident does not fall strictly within the terms of reference of this review which was intended to exclude incidents “in which contamination of drinking water is thought to have commenced more than a few days prior to detection”. The DWI nevertheless decided that it should be included. Its inclusion is useful for illustrating the type of investigation that can be carried out when the timescale of events is more protracted than is usual for incidents involving surface waters.

### Objective of study

The main objective of the study was to define precisely the nature of any illness related to phenol exposure. An additional objective was to determine if any illness occurred after exposure to phenol in water at concentrations below  $0.1 \text{ mg l}^{-1}$  (the EPA ‘emergency standard’ at that time).

### Design of study

The study was based on a comparison between three population groups, defined in terms of residential location and the results of water analyses, carried out between July 1974 and February 1975.

Group 1: all those living between 120 m and 310 m of the spill site and having at least one water sample with  $>0.1 \text{ mg phenol l}^{-1}$

Group 2: all families living adjacent to Group 1 (210 to 670 m from spill) who had between 0.001 and 0.1 mg phenol l<sup>-1</sup> in their water

Group 3: people living 1.9 km from the spill site and where well testing had detected no phenol in the water (distant control).

The study sample comprised most (91% of families) of the population available in these three groups.

The medical evaluation included a questionnaire covering 14 symptoms (completed by interviewer) and a brief physical examination giving special attention to eyes, mouth, skin and cutaneous sensation. Blood and urine samples were obtained from 50% of those examined, and tested for a range of determinands.

These investigations all took place in February 1975, some seven months after the incident. Water samples were obtained from the homes of participating families (in addition to the sampling that had been carried out earlier).

#### Method of analysis and presentation

The results from the questionnaires were presented as symptom rates and compared between Group 1 and Groups 2 and 3 (combined) with the aid of Fisher's Exact Test. The onset of symptoms was also plotted against time.

The measured concentrations of phenol were described in the text and, for Group 1 houses, tabulated.

#### Main findings

There were 39 persons in Group 1 (the study group), 61 in Group 2 and 58 in Group 3. No significant differences were noted in symptom rates between Groups 2 and 3 and so these groups were combined (controls). Diarrhoea, mouth sores, dark urine and burning mouth were reported by significantly more persons in the study group than in the combined control groups ( $p < 0.01$ ).

There were no significant differences between the study and control groups on physical examination nor on the laboratory tests on urine and blood.

#### Authors' interpretation

The excess of symptoms amongst the study group is consistent with phenol poisoning. The illness appears to have occurred only in those exposed to more than 0.1 mg l<sup>-1</sup> of phenol in water and to have had no long-term consequences.

#### Commentary

This is a competent study based on good analytical and medical data. Compared with some of the acute incidents on surface water, the water quality data available in this study are much more satisfactory. The medical data, based on interview and physical

examination, are more objective than those obtained elsewhere by self-administered questionnaires. The researchers for this study, however, had two advantages on their side: the small population affected and the relatively slow evolution of events. Investigative measures could therefore be thought-out within the timescale of the incident.

It can be said that the study met the authors' main objective. It would also have met the Department's primary objective and Objectives (ii), (iii) and (iv). Although the results gave no indication of illness after exposure to phenol in water at concentrations below  $0.1 \text{ mg l}^{-1}$  (authors' additional objective), it is not clear how strong a conclusion can be drawn on this, because there is insufficient information about the concentrations to which the subjects in Groups 2 and 3 were actually exposed.

Because this was a study in which measurements were made on effectively the whole population involved, and the subjects were interviewed separately, it largely avoids the pitfalls of recruitment bias and non-independence of responses, which have been noted in relation to several other studies.

## **B11 ELECTROPLATING PLANT, CANADA, 1987**

### Source of information

Sunderman *et al* (1988)

### Outline of incident

In a metal plating factory, an evening shift reported for work at 1 p.m. on Sunday 14th June. After 3 p.m. several workers on a nickel-plating production line began to feel ill with symptoms that some attributed to bitter tasting water from a drinking water fountain.

The supervisor on the night shift tested water samples from seven drinking water fountains. The sample from the suspect fountain was green and contained approximately  $2 \text{ g l}^{-1}$  nickel while the samples from other fountains were colourless and uncontaminated with nickel. The water supply to the contaminated fountain was flushed and disconnected at 3 am on Monday 15th June.

The nickel (as nickel sulphate, nickel chloride, boric acid) contamination of the drinking water was traced to a back-siphonage from a water recirculation system that cooled filtration pumps for the nickel-plating tank.

### Objective of study

The authors did not specify their objective, although it appeared to be to describe and quantify the illness associated with the ingestion of the nickel contaminated drinking water.

### Design of study

The study included all workers who had attended the factory between Sunday afternoon and Monday morning. 43 subjects were divided into three groups:

- Group A - 21 exposed workers who were examined the next day, on June 15. (This was subdivided into two groups A1 and A2 depending on whether they had been admitted to hospital. A1 included those individuals who had been admitted).
- Group B - 11 exposed workers who were not examined until 17th June
- Group C - 11 controls on the same production line who did not drink from the contaminated fountain

All the subjects were men. Information on their age and health status was obtained and follow-up studies were performed 6 weeks post-exposure.

A sample of water collected from the fountain on Sunday evening June 14th was analysed for nickel and boron. Also, specimens of urine and serum were collected from the subjects on 15, 16, 17 or 19 June and analysed by routine urinalysis and haematology tests. The ten workers who were admitted to hospital had additional medical tests.

### Method of analysis and presentation

The results were broken down into discussion of the:

- Incidence of symptoms reported by the symptomatic workers
- Nickel concentrations in body fluids of all the study groups
- Elimination half-lives for groups A1 and A2
- Diagnostic tests of all study groups
- Clinical course of the illness reported by symptomatic workers.

The methods of statistical analysis used were mainly descriptive (means, standard deviations). A simple linear regression model was used to relate the concentration of nickel in serum to the concentration in urine.

### Main findings

The water sample which was taken on the evening of the incident contained 1.63 g l<sup>-1</sup> of nickel and 68 mg l<sup>-1</sup> of boron. The estimated oral intake of nickel by the 20 symptomatic workers ranged from 0.5 to 2.5 g; the estimated oral intake of boron ranged from 20 - 100 mg.

There were 20 symptomatic workers of which 10 were from groups A1, 8 from A2 and a further 2 from group B. The incidence of the 13 symptoms described by these individuals was given as well as a general description of the initial clinical observations seen in symptomatic individuals.

The mean nickel concentrations which were measured in the serum and urine for the different groups on days 1, 2, 3 and 5 after the exposure incident were compared. The exposed groups, in particular group A<sub>1</sub>, had higher nickel concentrations in these body fluids than in the controls.

The elimination half-life of nickel was significantly shorter for group A<sub>1</sub> who had received diuresis compared to A<sub>2</sub> who did not. Diagnostic tests revealed that three subjects may have experienced mild, transient nephrotoxicity although results of the other urinalysis assays that were performed indicated no significant difference between exposed and control groups.

Subjects in Group A<sub>1</sub> were found to have slightly diminished temperatures on days 2-4 following exposure. No abnormalities were detected in the workers who returned for follow-up examination.

#### Authors' interpretation

The authors' interpretation centred on describing whether the symptoms that were reported following the consumption of the contaminated water were associated with nickel poisoning. The authors concluded that the illness had been associated with drinking nickel-contaminated water and that boric acid which had also been present in the water had not contributed significantly to the illnesses.

#### Commentary

This is an interesting and competently executed study, showing commendable promptness of organisation in response to the incident. The study must have been put into action almost immediately to enable collection of body fluids only a day after the exposure had taken place. The occupational setting of the incident and the small number of people involved undoubtedly helped the process of follow-up of all the workers who had been potentially involved. The report does not describe the method (interview, questionnaire) by which the symptoms were reported, nor how the estimates of oral intake of nickel were obtained. Presumably these estimates were based on the quantities of water that workers had consumed, but details were not given. There appears to have been no attempt to relate the concentrations of nickel in body fluids to the estimates of intake. This would have been interesting in addition to the relationship between the concentration of nickel in serum and urine. In spite of this omission the paper contains new toxicological information, arising from the unusual circumstances of the incident.

Although the authors did not make their objective as clear as they might have done, it can be said that the study met all of the Objectives (i-iv) under consideration in the present review.