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# THE HEALTH IMPACT OF THE BHOPAL DISASTER : AN EPIDEMIOLOGICAL PERSPECTIVE

BY

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Dedicated to the people of Bhopal who have suffered the consequences of the disaster and to the people from many walks of life who have responded to this great human tragedy.

" All scientific work is incomplete- whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at a given time. "

A.B.HILL.

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# CHAPTER 1

## INTRODUCTION

The world's most serious disaster in the chemical industry which occured at Bhopal, is a tragic instance of the adverse impact of chemical agents on human health. The health profession has historically more experience and expertise in dealing with biological and physical agents of disease. Experience with chemical agents was previously limited to small groups of workers in specialised occupations. Health problems arising therein were dealt with by specialised occupational health teams. With rapid growth of the chemical industry, there has been an increasing use of a variety of chemicals in activities of daily life as well as in agriculture. During the past decade there has been a growing realization that the adverse impact due to human interaction with chemical agents is now spreading beyond the confines of the workplace, to the environment and the public in general. Incidents at Bhopal (methyl isocyanate + ?), Seveso (dioxin), Mexico (butane) and Vietnam (Agent Orange) have demonstrated dramatic instances of these adverse effects. These events are often considered unfortunate, uncommon, freak events or accidents. However, they represent the tail end of the distribution of the more common, less serious, leaks, injuries and minor health effects resulting from exposure to chemicals. The long-term effects of lower dose and/or chronic exposure to several chemicals in use are at present unknown. However there is accumulating evidence of the adverse effects of some of them eg. the impact of pesticides on the environment and their effects on animals and man through the food chain.

The increasing use of potentially harmful chemicals, the conditions in which they are manufactured, the health and safety regulations adopted and implemented are closely linked to economic and political factors operating at a national and international level. People living and working in conditions of material poverty bear the brunt of the most adverse effects, because for them employment under any conditions is a necessity for survival. The poor also carry a double burden - suffering from the diseases of poverty viz. malnutrition and infections along with the modern diseases of industrialization. A balance sheet approach of costs and benefits to people has to be used in evaluating the role of chemicals in this context. The following quotation by Albert Einstein is relevant and must be kept in mind,

" Concern for man himself and his safety must always form the chief interest of all technical endeavours. Never forget this in the midst of your diagrams and equations".

Responsibility for the safety of workers and communities and the prevention of technological disasters requires the involvement of professionals and decision makers from several fields. More importantly it calls for committment and political will by wider forces in society. Public health physicians could contribute by using epidemiologic skills to study the health effects of these agents. This would help provide a firm basis of knowledge about possible effects on health, which could then be used for creating awareness and for policy making. This has already been recognised and interest in environmental epidemiology, which includes the above group of agents has been growing. Being a new area of enquiry, the limitations of the existing tools of research, have also to be kept in mind.

The chemical accident at Bhopal has been an experience of a public health emergency caused by a technological disaster. The World

Health Organization has defined a disaster as " an event that suddenly overwhelms the capacity of the normal system to respond" (Wasserman, 1985). Though used to describe natural disasters like earthquakes, floods and volcanoes the definition could also apply to technological disasters. In Bhopal, the disaster overwhelmed the capacity of individuals, physically and psychologically. And because of the magnitude of the numbers involved and its complexities it also overwhelmed the capacity of the macrosystem ie. the social and administrative structures to respond. Technological disasters are very complex and require specialist intervention. Besides the possibility of causing external bodily harm, they may also act at a cellular and biochemical level causing a disruption in physiological functioning leading to unknown pathological states.

Exposure of the population to toxic chemical vapours during the Bhopal disaster has resulted broadly in three adverse outcomes : mortality, morbidity and disability. An epidemiological perspective and method of study is vital to understanding the pattern and distribution of the three adverse outcomes in the community. Epidemiological studies and population profiles can provide data which could be used for various objectives viz.

a) to substantiate/support, disprove or provide clues for aetiological hypothesis.

b) following from the above, to help indirectly in deciding upon rational therapeutic interventions and in initiating secondary and tertiary preventive measures where possible.

c) to plan health services, including rehabilitation, for the affected people.

d) to provide supportive evidence in court, regarding extent of injury, in claims of compensation for the victims.

## CHAPTER 2

## OBJECTIVES

2.1 The **objectives** of this study are :

A) to review the available literature concerning the health impact of the Bhopal disaster viz.

- a brief review of the event itself,
- mortality following the exposure,
- morbidity following the exposure.

The latter two would include clinical observations and findings reported by medical professionals and the findings of a few epidemiological studies that were conducted.

B) to use an epidemiological perspective in the appraisal of the above information.

C) to review literature regarding the chemistry and toxicology of the "agent" ie the chemical substances that were released during the event which produced the adverse health effects.

D) based on all the above information, to discuss methodological issues relevant to an epidemiological approach to studying and understanding the adverse health outcomes following exposure to the toxic chemicals in Bhopal.

## 2.2 General comments :

In the context of an epidemiological perspective of the health impact, one must initially consider all available information in broad categories of the epidemiologic triad of agent, host and environment and also in terms of time, place and person. In the Bhopal situation, there were and still are several limitations in attempting this, since there are big "knowledge gaps" about the chemical agent/s of exposure and also about the possible outcomes on human health. These will be considered in greater detail later.

The situation in Bhopal is also complex in other respects. The incident has enormous medico-legal implications. There has been a delay in publication of results of ongoing studies. It has therefore not been easy to get adequate published references from standard scientific journals. For the purpose of this study a wide variety of secondary sources of information have been used to build up an epidemiological profile.

## 2.3 Sources of information used

These could be broadly classified as follows :

a) Articles published in journals. Many of these are toxicological studies and a few are reports of epidemiological studies.

b) Reports of the Indian Council of Medical Research (ICMR) that were available in the first 6 months following the disaster. Some of these are minutes of meetings at which many of the researchers presented their interim findings. Furthur reports / results of studies conducted are not available.

c) Reports of studies and investigations carried out by research teams not linked with the ICMR.

## CHAPTER 3

## THE DISASTER - A BACKGROUND

### 3.1 The event

The "Bhopal disaster" as it has come to be known, was a major leakage of toxic chemicals from a pesticide plant in the city of Bhopal on the night of 2/3 December 1984. The plant, Union Carbide India Ltd (UCIL), was the Indian subsidiary of a multinational chemical company, Union Carbide Corporation Ltd.(UCC), with headquarters in Danbury, Connecticut, USA. The leak occurred from a tank containing methyl isocyanate (MIC). It resulted in death and injury to human, as well as to plant and animal life.

### 3.2 The UCIL plant

The plant was set up in 1969 and gradually expanded over the years into a large manufacturing facility for the formulation of carbaryl, an insecticide, commercially known as Sevin. Till 1979, methyl isocyanate (MIC) and alpha naphthol, intermediates used in the manufacture of carbaryl, were imported from the parent company. Subsequently, from 1980, MIC was manufactured locally with knowhow and basic design supplied by UCC.

### 3.3 The manufacturing process

Very briefly the process for the manufacture of carbaryl is as follows : carbon monoxide is made to react with chlorine to yield phosgene which is then made to react with monomethylamine to produce methyl carbamoyl chloride. This is pyrolysed to yield methyl isocyanate and hydrogen chloride. Chloroform is used as a solvent and caustic lye for the neutralization of any toxic material. Finally MIC is made to react with alpha naphthol, in the presence of a catalyst and carbon tetrachloride as a solvent, to produce carbaryl. Different

concentrations of this are used to formulate the end products.

### 3.4 Carbaryl

Chemically known as 1-naphthalenol methyl carbamate, carbaryl is an insecticide which is " moderately hazardous" according to the WHO classification of pesticides. In 1976, the Environmental Protection Agency of the U.S.A placed it on the list of compounds that are " hazardous to man and environment". Carbaryl has been found to be toxic in some animal studies (Phoon,1986).

Alternative processes not requiring MIC, are available for the manufacture of carbaryl. They are in use by other companies who wanted to avoid the use of MIC, which was known to be hazardous chemical. However, they are more expensive and also produce larger volumes of waste material.

The MIC plant at Bhopal has had a track record of previous spills and accidents ever since its inception. In late 1981, one worker was killed and 3 injured from exposure to phosgene. In 1982, 18 workers were exposed to a mixture of three chemicals including MIC during a leak. The issue regarding inadequate safety measures - both in design and management practices - had been raised by the workers union, a local journalist, a safety commission from the US and even in the local legislative assembly (Agarwal, 1986 and Weir, 1986). However no action was taken.

# CHAPTER 4

# THE AGENT

## 4.1 Chain of events

The leakage occurred from an underground, stainless steel tank, in which 42 tonnes of liquid methyl isocyanate (MIC) had been stored from Oct 1984. Post disaster, the huge stainless steel tank was found to have bulged at the end and between the ribs. Part of the tank had risen out of the ground fracturing the concrete in which it was embedded. All this is evidence of a tremendous build up of pressure and temperature inside the tank - with temperatures possibly as high as 250 to 350oC and pressures upto 11-13 kg/cm2 (Varadarajan,1985).

Knowledge of what triggered the explosive "runaway" reaction, the type of chemical reaction that occurred and what products were formed is partly speculative.

The Indian Council of Scientific and Industrial Research (CSIR) have produced a detailed report about the possible chemical reactions that could have occurred. This is based on -
an analysis of contents of the tank; existing though limited knowledge of the chemistry of the substances involved and on laboratory experiments.

Some of the factors that contributed to the chain of events that took place are as follows (Varadarajan, 1985):

- the inherent chemical properties of MIC, especially its high reactivity and volatility, which will be described later.
- the storage of large quantities of MIC in very large size containers for long periods of time.
- insufficient caution in design, choice of materials for construction, and in the provision of measuring and alarm instruments.
- inadequate controls on systems of storage and on quality of stored

materials.

- inadequate guidelines and practices in operations and maintenance.

The probable chain of events that took place was :

- the entry of water and the presence of catalysts initiated an explosive, runaway, trimerization reaction with a rapid rise of temperature. A large portion of the stored liquid MIC vapourised with a rapid rise of pressure.

- carbon dioxide produced by the reaction of hydrolysis caused a mixing of contents in the tank leading to rapid chemical reactions.

- secondary chemical transformations occurred at the high temperatures reached, leading to the formation of a complex mixture of chemical substances. The following 12 products were found as residue in the tank : methyl isocyanate trimer, dimethyl isocyanurate, dimethyl urea, trimethyl urea, dione, trimethyl biuret, monomethylamine, di and trimethylamine, chloride and metallic iron.

A description of the properties of MIC only will be given, for the purposes of this report, to indicate the hazardous nature of the chemicals involved. MIC was probably present in large quantities in the cloud of toxic gas and it has also been the focus of most of the research effort. Hence some information about its chemical properties and toxicology is available. However it must be kept in mind that other chemicals could also be playing a causative role in the morbidity manifesting in the affected population. This could occur due to: other chemicals having been formed during the runaway reaction itself; and/or by the breakdown products of MIC in contact with the atmosphere; and/or by the reaction/biotransformation products of MIC in the human system.

4.2 **METHYL ISOCYANATE (MIC),**

isocyanic acid-methyl ester, $CH_3-N=C=O$,

**Chemical properties :**

MIC is mainly used as an intermediate in the production of Carbamate insecticides and herbicides eg. carbaryl (Sevin), aldicarb (Temik), carbofuran (Furadan) and propoxur (Baygon). MIC has a known hazard potential because of its ready volatility, low boiling point, flammability and high reactivity. Traces of metallic impurities act as catalysts and stimulate a violent exothermic polymerization. The heat generated can volatilize a large proportion of MIC. The gas has a very high inhalation toxicity. Hence extreme precautions are necessary in the production and handling of MIC

MIC has a low boiling point of 39.10C at 760 mm Hg. It is slightly lighter than water, but the gaseous form is heavier than air. Its vapour density is 1.97 as compared to 1.0 for air. It has a high vapour pressure of 348 mm Hg at 20oC. Because of these properties MIC vapour will be concentrated near ground level and have a greater impact on people, plants and animals.

The Mol.wt. is 57.05 and Sp.gravity 0.96 at $20^{oc}$.

Explosive limits :5.3 % and 26 % by volume air.

It is an extremely reactive substance. In the presence of water, hydrolysis occurs and monomethylamine (MMA) is produced ; one mole of MMA then reacts with another mole of MIC to form 1,3-dimethyl urea (DMU) with the generation of heat, or 1,3,5-trimethyl biuret (TMB) if there is excess MIC. At 73 % relative humidity MIC can decompose into monomethylamine.

Isocyanates in general react with carboxylic acid to generate a peptide bond with the liberation of CO2. They are also known for carbamylation at the biochemical level.

MIC reacts with itself and is known to polymerize on storage

for long periods. In the presence of a large number of metals and other catalysts a violent exothermic polymerization reaction occurs. It also reacts with hydroxyl compounds, amines and acids.

On heating and burning it generates several toxic decomposition products viz. nitrogen oxides, hydrocyanic acid and carbon monoxide.

The ACGIH (American Committee of Government Industrial Hygienists) have set the Threshold Limit Value (TLV) for MIC to be 0.02 ppm (0.05 mg/m3) for skin. The OSHA (Occupational Safety and Health Administration) Permissable Exposure Limit (PEL)is 0.02 ppm.

Salmon et al (1985) found that MIC vapour reacts only slowly with water vapour. Hence substantial amounts of MIC would be present in a vapour cloud released even into moist air. This would allow time for MIC to react with its own hydrolysis products.

In air MIC hydrolyses to CO2 and a relatively inert amine. It reacts in sunlight to form alkanes, nitrogen and carbon monoxide. If moisture is present it converts to MMA, DMU and TMB. With moist soil it forms methylamine which strongly adsorbs to the soil surface until degraded.

On contact with plant, animal and human tissues MIC has severe corrosive or irritant action. It is thought to compete or interfere with CO2 during photosynthesis. In animals and humans it is thought to transform to methylamine, CO2 and other carbamyl derivatives.

Thus, the chemical composition of the agents causing the adverse health effects in Bhopal are not yet completely known, nor their mechanism of action fully understood. More work needs to be done regarding breakdown products of MIC in conditions of high temperature and pressure and of those formed by hydrolysis. Their properties and immediate and long term toxic effects need to be studied. Experimental studies of animal exposure to MIC are described in a later section. Epidemiologic data could also provide clues regarding etiology.

## CHAPTER 5

## IMPACT ON THE BIOLOGICAL ENVIRONMENT

The toxic gas had an impact on animal and plant life as well as on soil and water. Most data quoted in this section is from the report by Agarwal (1986)

Official sources put the number of dead animals - cattle, goats, sheep etc at 1,047, while about 7,000 received therapeutic care.

An investigative team from a research institution found that animals had died within 3 minutes of inhaling the gas. They were frothing from the mouth, lacrimating and breathless. Many cows miscarried. In clinically ill animals, there was a drying of milk after the exposure. Milk production came down from 8 - 10 kg per day to 0 - 0.5 kg per day. Poultry were relatively less affected for unexplained reasons. Many birds escaped death as well.

The effect of MIC on plants and soil was studied by the Central Board for the Prevention and Control of Water Pollution and the Indian Council of Agricultural Research. The "neem" tree commonly growing in the area was found to be a sensitive atmospheric indicator. A vegetation damage contour map was drawn. Vegetation in an area of 3.5 sq km around the factory was severely affected, 10.5 sq km beyond that was badly affected, a further 6 sq km moderately and 5 sq km mildly affected. Leaves bore the brunt of the damage. Scientists found that there had been instant death in exposed tissues. Another study by the Benaras Hindu University found genetic defects in locally grown vegetables. The same species of plants which were otherwise badly affected were unharmed when found growing near the lake. Plants submerged in water were also unaffected.

Some clues for human epidemiological research from the above

account would be to study the effects on lactation in mothers, as it is of vital importance to the nutrition and health of infants, and to check mortality and morbidity near the lakes and beyond. Plant studies also confirm the gradient in damage at different distances from the factory, reflecting the gradient in exposure. The area affected, as given in the contour map, is much wider than the area considered to be exposed for human health effects.

The Health Dept. even reported a bright side of the disaster. Gas affected areas have recorded a reduction in the incidence of malaria. Mosquito breeding has apparantly been affected by MIC.

## CHAPTER 6

## THE HEALTH IMPACT OF THE DISASTER

### 6.1 The need for an epidemiological perspective :

When studying the health impact of the Bhopal disaster, we are faced with a situation where the cause of the presenting complex of symptoms and signs is partially unknown even at present. The long term effects on human health are also unknown. There is an urgent necessity to understand the toxicology and pathogenesis of the agent/s involved so as to be able to provide rational therapeutic care and if possible to initiate secondary and tertiary preventive measures. Data needed would include facts about the clinical presentation of the disease complex, the pathophysiology of the affected and related organ systems, the analytical chemistry and toxicology of the agent/s.

The role of the epidemiologist would be to provide information about:

- the distribution of the new disease complex in the population,
- the characteristics of people who manifest these adverse health effects,
- the various circumstances which may predispose to the development of adverse effects,
- the morbidity attributable to the exposure as separate from pre existing levels of morbidity in the community by comparison with control groups of similar age / sex structure and socioeconomic status,
- to provide data relating different symptoms and signs to different degrees of exposure.
- to understand the natural history of the morbidity over time,

I shall commence by describing available data in the

epidemiological categories of time, place and person recognizing that the three are intrinsically interrelated.

## 6.2 Descriptive epidemiology

An attempt has been made to build up a picture of the descriptive epidemiology of the event and its aftermath from available sources of information.

6.2.1 At the outset some of the limitations encountered by groups involved in carrying out medical work with the victims or in studying the health impact must be considered viz.

a) There was a lack of authentic information regarding the chemical composition of the cloud of vapours that escaped that night. The leak occurred from a tank containing methyl isocyanate following an explosive runaway reaction. Very little was written (and possibly known) about MIC, its reactions in different circumstances or its toxicology, in standard textbooks or journals. The company did not disclose information that it had accumulated in the process of registering for the commercial production of MIC. Thus medical professionals and research workers were handicapped by ignorance about the identity and properties of the agent whose effects they were trying to study and treat.

Speculations regarding possible agents ranged from MIC, phosgene, carbon monoxide, cyanide, cyanogenic substances and a combination of all the above and/or other unknown chemicals. These drawbacks in carrying out medical work with the victims have been reflected in the reporting of the clinical findings and also in the treatment given.

b) Details of the number of fatalities and of those affected are not precisely known. Because of the suddeness and magnitude of the disaster, mass burying/cremation of bodies (human as well as animal)

was carried out on an emergency footing, to avoid furthur public health problems. In the conditions of disaster and panic, with many of the staff themselves affected, routine administrative structures could not cope with the need for rigorous documentation vital for future treatment and compensation of victims and for the understanding of the epidemiology of the aftermath. Different sources, therefore, give varying estimates of the numbers who died and who were affected.

c) Because of the medico legal implications of the disaster a certain degree of administrative overcaution built up in the months following the exposure and results of studies of morbidity, toxicology etc. conducted by various research groups of the Government and the company were not made available to the medical community for scientific debate.

d) other factors which affected studies in the early phase were

- mass exodus of people from the affected areas away from Bhopal, during "operation faith" twelve days following the exposure, when the remaining MIC in the plant was "neutralised". The people subsequently returned to Bhopal over a period of time. Hence there is a variability in the baseline population in the different studies.

- migration outside and into the affected areas altering the population at risk. Most of the affected areas being shanty towns, many people had their roots in villages and towns outside Bhopal. A proportion of people migrated back to their hometowns or villages or elsewhere for treatment, jobs or for other reasons. Similarly, relatives of the victims also came into Bhopal to care for their families. This sort of social support during times of stress is very common in India. It has been claimed that a large number of unaffected people migrated into the exposed areas to claim compensation. Studies have not substantiated this claim. The occasional case reported must

be the exception rather than the rule.

- invasion by lawyers and other people created confusion and distrust among the people. This may affect the reporting of the history / symptoms to extents that would depend on the degree of trust / rapport created between the people and the research teams.

### 6.2.2 Time

The leakage occured on the night of 2/3 December 1984. The leak was first noticed at 11.30 pm in the MIC production area. Workers noticed some dirty water spilling from a higher level in the MIC production structure. They also felt the presence of MIC in the atmosphere by a sense of irritation in their eyes. Due to experience with previous minor leaks they were able to recognize the presence of MIC by its irritant effects. Water was sprayed around the point of leakage, as in the presence of water MIC converts to less harmful products. At 12.15 am indicators showed that pressure in MIC tank 610 was shooting up and by 12.30 am it went beyond the maximum on the scale ie. 55 psig. The temperature indicator was also beyond its range ie. + 25°C. The safety release valve popped out and a gaseous cloud was seen coming out of the stack which was 120 feet high. The siren was sounded around 12.30 am for a short while after which only the internal factory alarm was continued according to the routine practice followed in the factory. Water was sprayed to neutralise the MIC but could not reach the height from where the gas was emanating. Around 03.00 am the safety release valve of the tank is reported to have sat back and the gas stopped coming out of the tank.

Meanwhile, around 12.45 am people in JayaPrakash Nagar 100 yards south of the plant, woke up choking, coughing and with a burning sensation in their eyes, nose and throat - reported by the victims

"as if chilli powder was in the air".

At Bhopal's 1,200 bed Hamidia Hospital, about 3 km from the factory, the first patient reported at 1.15 am and then they came in thousands. It was around 3.00 am that the first deaths due to the gas leak were reported. There was a stampede as the populace began fleeing the city. People died in their homes, in the hospitals, and on the roads even upto some distance away from Bhopal.

This was the starting point for continuing morbidity and mortality in the exposed population over the next few days and weeks. Standard medical therapeutic practices were adopted. However, it was the experience of local medical practitioners that the exposed people came repeatedly to the clinics with a variety of symptoms and signs affecting several organ systems, apparently unrelated to each other. This continued beyond weeks into months.

Ten days following the disaster it was announced, that as a safety measure, remaining MIC in the two other tanks 611 and 619 were to be neutralised by conversion into carbaryl.This created a panic and despite assurances of complete safety, there was an exodus of people from the vulnerable localities. On December 13, 1984, 100,000 people left the city. Many took their animals too. By the next day a quarter of the city's population had fled. Many hospitalised patients also left. Cases of injuries and accidents in the virtual stampede during the fleeing of the city, occurred on both occasions, adding to the morbidity related to the disaster. The second exodus furthur aggravated the situation as it interrupted treatment, resulted in physical and psychological stress in those already affected and was also an additional financial burden.

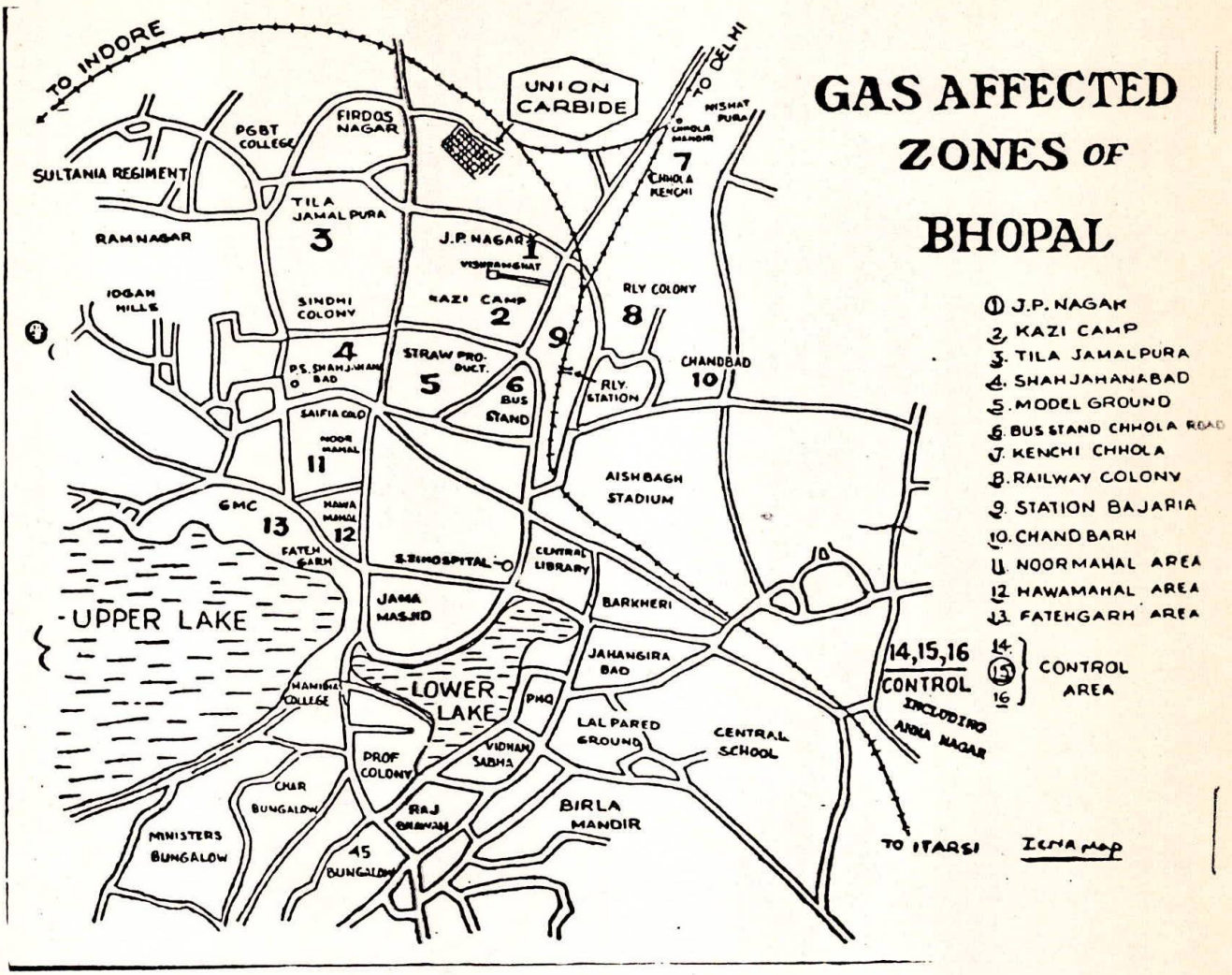
Generalizing broadly, the event could be described as an exposure of a population to an extremely toxic air borne chemical agent, with sharp localization in place and time. It resulted in a

large excess of deaths and disease frequency in the exposed population. This is characteristic of an explosive, acute, point epidemic. However there is evidence of continuing or persistent morbidity and suggestions of an excess mortality in the exposed population. Reasons for this are not completely understood. Several possible mechanisms have been proposed and will be considered later.

### 6.2.3 **Place**

Bhopal is the capital of the State of Madhya Pradesh in central India. The city has a population of about 800,000. The UCIL plant was located in the northern fringe of the city, adjacent to an existing residential area and barely 2 kilometers away from the railway station. Some squatter settlements did grow up around the Carbide plant after it was opened in the late 1960's. But some of the areas worst affected by the gas leak had been inhabited for many years before the Carbide plant opened.

The high vapour density of MIC along with the conditions of atmospheric inversion that winter night, caused the cloud of gas to move down and stay close to the ground. The vapours spread slowly in the atmosphere due to the low wind velocity. All these factors resulted in the population being affected greatly. The gas is reported to have spread over an area of about 40 sq.km and affected people seriously as far as 5 to 8 km downwind (see map). Classification of areas into seriously affected and less seriously affected were made on the basis of crude post exposure death rates in different localities. This was done by the State Govt. The most seriously affected areas were JayaPrakash Nagar, Kazi Camp, Chola Road, Chandbad, New Kabbad Khana, Sindhi Colony and Railway Colony (see map). The two lakes of Bhopal are said to have averted a larger tragedy as MIC converts to less harmful substances in contact with water.




SOURCE: ICMR map from Patel A and Patel A, (1985) The Bhopal disaster aftermath : an epidemiological and socomedical survey.

In studies of the Bhopal ... cohort, comparisons of place would have to be done between relatively small distances away from the factory, to test a dose response effect of varying degrees of exposure on the outcome. Geographical distance however would be only one among other indicators of exposure as will be discussed later. Despite known limitations of ascertainment and precision, routine sources of data regarding mortality ... would initially have to be used. Results of the few population based epidemiological studies would also be able to provide additional information. Preparation of maps showing the distribution of deaths

could be drawn. Relating these numbers to the denominator viz. the population who were exposed and hence at risk, would give crude death rates following the exposure, according to geographical area or locality. Baseline data of the population available from the census, electoral rolls or even by the surveys conducted after the disaster by Governmental agencies, could be used to calculate age and sex standardised mortality rates for different areas.

### 6.2.4 Person

This aspect will be discussed in terms of the population at risk, its demographic and other characteristics. The picture of mortality and morbidity will be described in later chapters.

#### a) Population at risk

Estimates of the total population exposed to the toxic gas or the "population at risk" for the derivation of mortality and morbidity rates are 200,000 according to the State Government and UNICEF. Results from epidemiological, community based studies (Patel et al,1985 and Nagrik study, 1985) using control groups 10 kms away from the factory, suggest that even the control groups were mildly affected by the exposure. This indicates that the basis for defining the "exposed population" needs furthur substantiation. This will be dealt with again in the discussion on the exposure variable.

The factor of post exposure migration into and out of the exposed localities would have also affected the composition of the population at risk. Andersson et al (1985) observed that the more seriously affected had gone back to their hometowns or villages. Sathyamala C (1986), found that in a population of 8159 surveyed in Sept. 1985, 43 people (0.52%) moved in after the gas leak and 41 (0.50%) had moved out. Both the above movements would result in an

overall dilution effect or underestimation of morbidity . Though quantitatively this may not be of a large order (1% in the above study) it must be kept in mind that the qualitative difference may be important if those who were seriously ill had gone away.

New births into the population and deaths (fully, partly or not attributable to the exposure) would also alter the baseline population. Since households have been generally used as the sampling units in the studies conducted so far, this factor has not been considered at the sampling stage. However it would alter the number and composition of the baseline population and would affect the calculation of rates.

Patel et al (1985) extrapolating from prevalence rates of morbidity have estimated that, of the exposed population about 70,000 would be suffering from serious health effects while 45,000 would be suffering moderate to mild effects.

b) **Demographic characteristics**

UNICEF officials (Agarwal A 1985) estimate that, of the affected population :

- 75% are slum dwellers ie. from the lower socioeconomic strata;
- 80% are Muslims;
- 40% are children below the age of 15, 10% are elderly and
- 20% are women in the reproductive age group.

The basis of this analysis is not known. It was probably done as an estimate for planning and administrative purposes. The demographic data appear to be direct extrapolations from national figures. This would be very inadequate data for a thorough understanding of the aftermath.

Banerji et al (1985) have described the socioeconomic profile of the study population as follows :

Muslims : 30%, Lower castes : 20%, Backward castes : 18%

Income of Rs 150/head/month ( ie relatively well off) : 10%

Housing : Kutcha (without brick and cement) : 70%

Pucca (well built/concrete) : 30%

Presence of holes in the structure : 50%

(allowing air entry)

Patel et al (1985) found the population to be predominantly Muslims and Harijans in JP Nagar and Tamilians and Maharashtrians in Anna Nagar.They belonged to the lower socio economic class - the percentage of skilled workers being less than 10 %. The range of occupations included daily wage labourers, construction workers, beedi rollers, cobblers, railway and factory employees, domestic workers, self employed artisans and potters.

The profile is of a population, the majority of whom belong to the lower socioeconomic class. The poor housing conditions would have offered no protection from the toxic chemicals in the atmosphere.

c) Community awareness of the hazard potential of the plant

Most people had no idea about the hazardous nature of the plant operation. Banerji et al (1985) report that the population were not told earlier of the potential hazard of the plant. Nor were they aware of preventive measures to be taken in case of a leakage eg. use of a wet cloth, moving in a direction away from the wind, not running etc. Unfortunately most of them ran in the direction of the wind carrying the gas and were furthur exposed. A Patel et al (1985) found that 8.3% of the population in JP Nagar and 0.08% in AnnaNagar took safety measures at the time of the disaster. Most of these reported to having used blankets/wet towels over the face by instinct rather than due to prior knowledge. The workers in the plant knew of these precautions and all those in the night shift escaped unhurt, except

one.

d) **Pattern of utilization of health services**

Banerji et al (1985) found that the utilization of health services by the study population after the exposure was as follows :

| | |
|---|---|
| Hospital | 40.2 % |
| Camps | 46 % |
| Dispensaries | 2.5 % |
| General practitioners | 25 % |
| Registered medical practitioners | 2.5 % |
| Institutions outside Bhopal | 9.1 % |

There is an overlap as some people utilised more than one type of service. These findings are an indication that when studying the distribution of disease in the community, data collection would need to be population based to get a true picture of morbidity. When using hospital or clinic based data one would have to keep in mind selection bias caused by selective attendance of patients. Possible determining factors for this could be severity of illness, accessibility of service, social class of the affected persons and so on.

e) Impact on income

Patel et al (1985) found that 65 % of wage earning individuals in the exposed group experienced a drop in income ranging from 20 % to 100 % with a median of 50 %. In the controls, only 9 % reported a drop in income in the range of 20 - 55 %. This occurred due to physical ill health resulting in occupational disability.

# CHAPTER 7

# MORTALITY

## 7.1 Exposure related mortality rates

There is uncertainty as to the exact number of people who died. In its petition in Court, the Government has claimed 1,700 dead. This is based on death certificates issued/deaths recorded by Government authorities.

The Indian Council of Medical Research report (1985) states that about 1,200 people died in hospital wards. They estimate the total death figure to be about 2,000. The maximum number of deaths were recorded in JP Nagar, Kazi Camp, Kenchi Chola and Railway Colony. These areas accounted for 777 deaths.

They quote a study done soon after the disaster, in which 300 families consisting of 968 males and 863 females were surveyed. 47 deaths in males and 35 deaths in females were recorded ie. the crude post exposure death rate for this population was 48.55/1000 population for males and 40.55/1000 population for females. The maximum mortality was in the 0 to 5 year and above 60 year age group. Most deaths occurred within 48 to 72 hours of the disaster. No details are given of exactly how long after the disaster this study was done, from which population the families were drawn, what the method of sampling was or details of the age structure of the population or the dead.

Andersson et al (1985), in an epidemiological study, conducted during the first 10 days after the disaster, found the crude death rate derived from households in the worst affected population based cluster to be 3% or 30/1,000 population, (death rates being calculated as number deceased/number exposed). They have stated that this data

would confirm estimates of a total of 2000 - 2500 exposure related deaths. Random sampling methods were not used and exact location of study areas have not been mentioned. However extrapolation of rates from localised study areas to the total exposed population should be made with caution. Reasons for this will be apparent when summing up the results from the various studies conducted.

Patel A et al (1985), in another population based, cross-sectional study, using statistical methods for sample size determination and random sampling methods, found that the crude death rate was 86.6/1,000 population in JayaPrakash Nagar (01) and 7.9/1,000 in the control area of Anna Nagar (15)(refer to the map). The Dept. of Information and Publicity of the State Govt. had documented the death rates to be 23.4/1,000 and 3.2/1,000 respectively in the same areas. It appears that there is a gradient of mortality according to the degree of exposure. This is another reason why direct extrapolation of rates from any particular study/area to the total affected population may be misleading.

Banerji D et al (1985) conducted a survey in the affected areas, between Jan 6 to 15,1985. Using a sampling frame of 68,000, they randomly selected a 6.66% sample (1 in 15 households), and administered a semistructured questionnaire by trained interviewers. They enumerated 82 dead and 5 missing (presumed dead) in 700 households in the severely and moderately affected areas. The exact denominator has not been mentioned in their preliminary report, to be able to calculate rates. They extrapolated the number to their sampling frame of 68,000 to yield 1305 dead. From this study the crude death rate for the combined population of severely and moderately affected communities is 19.19/1,000 population. The exact area covered by the study has not been mentioned.

Beside the caution mentioned earlier regarding extrapolation

of rates, it appears that combining rates from different localities eg. severely and moderately exposed to give an overall rate may mask important differences in mortality rates.

Sathyamala C (1986), surveyed 3 exposed localities to study the impact of the exposure on the outcome of pregnancy. The basis of selection was the post exposure mortality rates as given in later unpublished data from the study by Banerji et al.. These were as follows :

JP Nagar - 65.3/1000, Kazi Camp - 46.7/1000 and Kenchi Chola - 35.7/1000. Their study found the crude post exposure death rate for the 3 localities together to be 33.19/1000.

A table of postexposure mortality rates as derived from different studies has been compiled. Relevant aspects of the study designs have also been given.

## Post exposure mortality rates
## A summary from different sources

| Study group/ investigator | Population/ sample size | Sampling method | Time of study | Area of study | Crudepost exposure deathrate |
|---|---|---|---|---|---|
| MP State Govt. | ? | ? | Early post disaster | JPNagar<br>AnnaNagar | 23.4/1000<br>3.2/1000 |
| ICMR | 300 families (968 males + 863 females) | ? | shortly after disaster | ? | 48.5/1000 (males) 40.5/1000 (females) |
| Andersson et al | ? number in each cluster | ? | 10 days post exposure | worst affected cluster | 3 % or 30/1000 |
| Patel A et al | 148 exposed 138 controls | Random sampling | 3 months post exposure | JPNagar<br>AnnaNagar | 86.6/1000<br>7.6/1000 |
| Banerji et al | 700 families | Syste-matic sampling | 1 month post exposure | severely + moderately affected areas<br>JPNagar<br>KaziCamp<br>K.Chola | 19.2/1000<br>65.3/1000<br>46.7/1000<br>35.7/1000 |
| Sathyamala | 8165 persons | Random sampling | 9 months post exposure | JPNagar Kazi Camp K.Chola together | 33.8/1000 |

There seems to be a wide variation in crude death rates derived from the various studies as well as in those stated by the Govt. Possible reasons for this could be :

a) differences in levels of ascertainment, reporting etc

b) due to factors related to study design - sample size, sampling methods etc

c) real differences in different localities reflecting varying levels of exposure to toxic gas.

The methods used in enumerating deaths would also play a role in accounting for differences between studies in postexposure death rates. Andersson et al (1984) have mentioned that they calculated death rates as the number deceased/number exposed. Other studies have not stated what they have considered and used in the numerator and denominator. The different studies were conducted at varying time intervals following the exposure. We do not know the time period used in the different studies as cut off points in the enumeration of deaths attributable to the exposure.

From an aetiological point of view, as well as for the victims families to receive adequate compensation, it is crucial to try and achieve greater precision in enumerating deaths. It is important also to analyse exposure related mortality rates taking into consideration age, sex, locality in which present at the time of the disaster and degree of exposure.

## 7.2 Demographic characteristics

Furthur details of the study by Banerji et al (1985) are given here as it describes the age/ sex and socioeconomic profile of the dead.

a) Males accounted for 60% of the deaths, which they commented was an important and unexplained finding. Majority of these were in the age range of 2 to 20 years. As a first step in interpreting these differences it is important to take into consideration the sex ratio and age distribution ie. the population structure, of the population at risk. As mentioned before, standardised mortality rates would be more interpretable.

b) There was one death per household in 49 households, two deaths/household in 11 households, three deaths/household in 4 households and one household had 4 deaths. There is a need to analyse these deaths in terms of degree of exposure.

c) In an attempt towards determining the degree of exposure it was found that:

- 75% of the dead were among those who ran on foot,
- 23.5% among those who remained at home,
- while none who used a vehicle died.

This is related to the finding that 73% ran, 21% stayed in their house and 6.3% used a vehicle. This is plausible because besides direct exposure to the toxic chemical laden atmosphere, those who ran also inhaled deeply and had an increased rate of respiration thus getting exposed to more of the toxic gas.

d) Among the dead the socio economic profile is as follows :

- 56% lived in houses with large holes,
- the proportion living in kutcha houses was higher,

- the proportion belonging to the lower and backward castes was significantly higher,

- the proportion of Muslims was similiar to that in the study population

ie. those who died were the poorest of the poor.

The few rich who came within the sweep of the cloud of toxic chemicals did not suffer as much damage " because of their well built houses, healthier bodies and possession of/access to transport."

e) The study hypothesises that there would have been an underestimation of deaths because of underreporting of deaths among the homeless and destitute who would have been the most exposed and vulnerable. An estimate of 3,000 shelterless in Bhopal has been made (Agarwal 1985). Many of these people used to live around the railway station which was directly in the line of the cloud of toxic chemicals.

The Tata Institute of Social Studies, Bombay, conducted a door to door survey regarding exposure, mortality, socioeconomic status etc the results of which were to become the basis for relief, compensation and long term treatment. But its total tally of 1021 dead, even less than the officially counted bodies caused it to lose credibility. The survey failed to cover 600 exposed families in which deaths could have occurred. It could not enumerate 315 families who had migrated outside the city after the disaster and 286 families who had their houses locked. The findings of the study, even with its limitations, would have provided some information of use. However the results have not been published or made available.

Many say that the official numbers are underestimates of the true figures of mortality. Other estimates have been given ranging from 7000 - 10,000 (Agarwal,1985). However most of this data is

anecdotal and hence difficult to interpret.

Regarding mortality in the months following the disaster, but attributable to the exposure, a State Govt.official has stated that during the first year on an average 15 such deaths were occuring per month (Diamond,1985). Whatever the basis and validity of this statement it raises the important question of the need to evolve a reliable method to take count of these attributable excess deaths.

The number of excess abortions and stillbirths should also be added to the death toll.

To summarise, therefore, the main features of mortality in the data reviewed are :

1) Number of deaths :

   estimates range from 1,700 - 2,500 - > 5,000.

2) Exposure related death rates :

   varies in different studies and in different localities

3) Area distribution

   severly affected areas - JP Nagar, Kazi Camp, Kenchi Chola and Railway Colony.

4) Sex distribution

   apparently an excess in males.

5) Age distribution

   excess in under 5 and over 60 age groups

  (age / sex estimates based on crude rates)

6) Socio economic class distribution

   lower socio economic classes most affected.

7) Excess abortions and still births occurred.

8) Continuing mortality attributable to exposure needs to be considered.

## CHAPTER 8

## AUTOPSIES

Autopsies were conducted at the Medico Legal Institute based at Mahatma Gandhi Medical College, Bhopal. Findings have been reported in the ICMR reports (Mar and May 1985) and are described in some detail here as they are of relevance to understand the pathology produced in the human system by acute, severe exposure.

### 8.1 The first week

The usual postmortem lividity or cyanosis was not present, but there was a pinkish discolouration. Conjunctiva were red. Hypostasis was present all over the body and was not restricted to the dependant parts. A common finding was the presence of thick, tenacious , foamy froth covering the nose and mouth.

Pathological changes were present in the entire respiratory tract. Lung weight was 2 to 3 times the normal. The lungs were waterlogged and had a cherry red colour. They showed congestion, haemorrage and consolidation. The vessels were filled with thick, viscid, dark cherry red blood. The bronchi and trachea were red in colour and the lumen was filled with white tenacious material. Microscopic examination showed severe tracheitis and bronchitis with denudation of the epithelium in some sections and necrotising bronchiolitis in some. There was marked congestion and thickening of the alveolar septa. The alveoli were filled with albuminous fluid. There was very little evidence of secondary infection.

### 8.2 The second week

While grossly and microscopically the lungs continued to be the seat of primary change, there was a gradual transition in the pathological changes. Characteristic cherry red colour of the blood,

heavy oedematous darkly reddish lungs and varying degrees of oedema of the brain continued. Acute desquamatous changes in the trachea and main divisions of the bronchi persisted. There were varying degrees of bronchiolitis, bronchopneumonia and infiltration of the alveolar spaces by polymorphonuclear cells.

In the acute phase there was oedema of the brain and congestion of the leptomeninges. In a few cases, the liver showed a mild degree of fatty change which can be either incidental or secondary to anoxia consequent to pulmonary changes.

## 8.3 The third week

The respiratory tract showed the same appearance, though the lungs were relatively reduced in size and weight. However they were still reddish and exuded a lot of fluid from cut surfaces.

A striking feature in some cases was that on opening the thoracic or abdominal cavities, viscera which was normal in colour rapidly acquired a reddish tinge on coming in contact with the atmosphere. There was variable involvement of other viscera. Brains, which were uniformly heavy and oedematous, showed either uncal grooving or tonsillar herniation with compression of the cerebellum by the tentorial edge. In a few cases the liver showed severe congestion. The spleen though markedly congested was shrunken in size and the capsule was wrinkled. The kidney showed extreme congestion in the cortex and medulla. The heart contained blood clots which were cherry red with some chicken fat like material. The liver showed haemorrhage all over. The capsule of the liver was found to be separated and could be easily pulled off. The gallbladder was distended. The stomach and intestines had haemorrhages in the submucosa of the wall. The spleen was found to be softened. The kidney showed haemorrhages.

8.4 Histopathology

The lungs showed congestion and oedema. The bronchial lumen was full of exudate. The trachea showed superficial ulceration and loss of cilia. Muscle fibres in the bronchial wall showed fragmentation. The kidneys showed necrosis of the proximal tubules. Microthrombi were present. The liver showed centrilobular congestion, patchy necrosis and widening of the central veins. Heart showed interstitial oedema and necrosis. Atrophy of the malpigian capsule was a consistent finding in the spleen. The cornea showed denudation of the epithelium. The thymus ,testis and ovaries showed no changes. Multiple lesions were common. Sections of the lungs of stillborn showed no abnormalities.

They quote the case of a woman who had manifested MIC effects and subsequently recovered. She died of hyperpyrexia following a Caesarian section in the third week of March 1985. On autopsy (on 29.3.85) lungs showed congestion, oedema and haemorrhage, and the small bronchioles showed obstruction. There was no pontine haemorrhage.

**Electron microscopic findings from autopsies**

Lungs showed loss of lining membrane of the epithelial cells. Type 11 pneumocytes were present indicating that capacity for regeneration was not totally lost. Red cells looked different- they had lost their electron opacity. This could be because haemoglobin is lost or a change has occurred in the structure of the haemoglobin. Several areas showed zones of activated fibroblasts. Some lungs showed secondary bronchopneumonia. The brain showed presence of siderosomes. Neurones showed flocculent opacity indicating necrosis. Examination of one placenta showed loss of microvilli on the maternal side of the syncitial trophoblast.

# CHAPTER 9

# MORBIDITY - CLINICAL FINDINGS

## 9.1 General comments

A profile of the morbidity caused by the exposure has been compiled from the following sources of information :

a) the two reports by the Indian Council of Medical Research (ICMR) in March and May 1985 describe the clinical picture and results of laboratory investigations in the acute and subacute phases. These observations were made by staff of the local Mahatma Gandhi Medical College at its attached Hamidia Hospital as well as by specialists sent in from other parts of the country. Several research projects (22-25) were set up by the two organizations in the initial phase for long term follow up of the victims. However further reports of their findings or progress are not available.

b) studies done by non-governmental groups. These include research teams from academic departments of universities, independent professional groups and voluntary agencies.

The clinical picture of morbidity is described first followed by the epidemiologial studies. Comments on the strengths and limitations of the data are interspersed with the description. There will be a further discussion of methodological issues later.

The pattern of morbidity varied over time. For the purpose of this report the acute phase has been considered as the first 2 weeks post exposure. The subacute phase is from 2 weeks to 4 months and beyond that period is the chronic or long term phase. This classification is arbitrary and partly artificial to help understand the clinical picture over time.

The most striking symptoms and signs with which most people presented immediately after the disaster or in the acute phase were

related to the eyes and respiratory tract. There were also a wide variety of clinical symptoms related to different organs and systems.

A description of the clinical findings in the acute and subacute phases follows.

## 9.2 ACUTE AND SUBACUTE PHASES

### 9.2.1 The eyes

Mittal (ICMR, 1985) reported the following eye conditions in patients from the hospital OPD and wards of Hamidia Hospital. 8,000 patients were seen here in the first 24 hours, and 34,000 patients were treated in the first few weeks.

Patients initially complained of a severe burning / foreign body sensation in the eyes, blurring of vision, profuse lacrimation, and difficulty in opening the eyelids. On examination there was lid oedema. 60 - 70 % had superficial keratitis and conjunctivitis. Superficial ulceration of the cornea in the interpalpebral region was observed in several cases. Many had punctate keratitis in the lower sector. Corneal pathology was mainly confined to the epithelial layers, rarely penetrating the stromal tissues. They observed that children had fewer ocular problems. Eyes of nearly all the patients returned to near normal in a weeks time with healing of the lesions. Detailed investigations did not suggest involvement of the posterior chamber. There was no evidence of blindness or deterioration in vision.

Andersson et al (Dec'84) reported findings in 10 hospitalised patients on the eighth day post exposure. All had discrete superficial lesions, usually in a band across the interpalpebral region with the typical whorling pattern of new epithelial growth. No limbal necrosis or abnormal endothelium was detected. Their findings were in keeping

with the report given above.

Andersson et al (Dec'84) also reported findings from a study of community based clusters, 2 weeks post exposure. The exact location and distance of the clusters from the factory were not specified. They reported that over half the community demonstrated eye signs which could be attributed to the exposure. These were mainly interpalpebral injection and signs of healing epithelium. Fundal changes, mostly venous dilatation were more common in the exposed. There was no difference in the age standardised visual acuity between exposed and unexposed groups.

A.Bang (Jan'85) reported that in the week after the disaster a quick and crude community survey in JayaPrakash Nagar (100 yards from the factory) revealed that about 50% of the population had eye symptoms.

The Nagrik study (1985), found that 80% of people within km of the factory had ophthalmic symptoms, as did 60% of those at 2 km and 40 % of those at a distance of 8 km. This revealed a gradient of effect as well as the fact that exposure occurred even upto 8 km away.

### 9.2.2 The respiratory system

The ICMR report's (1985) state that people initially complained of sudden onset of difficulty in breathing, coughing and in some cases, pain in the chest. On auscultation, many had bilateral crepitations. Xrays revealed interstitial pulmonary oedema, alveolar type oedema, pneumonitis, hyperinflation of lungs and collapse of surrounding area. Rapid deaths following exposure probably resulted from massive pulmonary oedema and associated hypoxia.

A.Bang (1985) in the survey mentioned above, found that about 25% of the population in JP Nagar had respiratory symptoms. A large number, even those with minimal respiratory symptoms had coarse

crepitations and rhonchi. Many of the" mild" cases were either not attending clinics or were not being given a thorough clinical examination. He pointed out that with inadequately designed studies and poor documentation the real epidemiology of morbidity may be missed. He also observed that the expected tide of secondary infection did not follow the initial period of chemical pneumonitis. Reasons for this were not understood. At the community level, antibiotic cover was either not given or was too inadequate for most of the affected persons and hence could not explain the phenomenon. There are also anecdotal observations that dead bodies of people / animals discovered a day or two after the disaster were not decomposing. On experimental studies (ICMR,1985) MIC was found to have a bactericidal effect.

Andersson et al (1985) observed that respiratory distress was most marked in the community cluster "second in distance from the factory", affecting 20 % of the population. Many were too disabled by breathlessness to move more than a few steps or even to talk.

S.R.Kamat et al (ICMR,1985) noted on 24 subjects, ( a self selected group who had gone to Bombay for treatment shortly after the disaster ), that lung function tests suggested restriction, reversible obstruction and defects in oxygen exchange. Blood gas analysis revealed anoxia, compensatory respiratory alkalosis, raised carboxyhaemoglobin and methaemoglobin. They reported evidence of lymphoid granulations in the throat.

They later reported findings from an extensive evaluation of pulmonary function of 82 patients (also self reporting to Bombay). Xrays in 78 were suggestive of interstitial pneumonitis. This was corroborated by blood gas and lung function studies. Methaemoglobin levels were raised in 63 out of 80 and was stated to be suggestive of interstitial alveolitis. Pulmonary function tests indicated central airway obstruction. A large majority of the 82 also showed some

of respiratory symptoms had ventilatory impairment, 12% had restrictive lung disease, 6% obstructive airway disease and 22% obstructive cum restrictive defect. Ventilatory defects were not observed in patients with mild exposure to toxic gas.

The ICMR report (1985) states that of 35 patients in whom blood gas analysis was done, 23 severely exposed patients had arterial oxygen tension (PaO2) less than 60 mm Hg ie. moderately low levels. Moderately and mildly exposed patients had normal PaO2. Low arterial carbon dioxide tension ( less than 35 mm Hg ) was observed in 12 cases. It was stated that these results indicate significant alteration in blood gases and suggest alteration in oxygen carrying capacity of the blood.

Narayanan (ICMR,1985) reported, from experience in a 30 bedded, hospital set up adjacent to the factory and hence more accessible to the affected people. The exposed population were presenting with recurring respiratory problems. They also complained of inability to perform accustomed physical activity. They had tachycardia and severe tachypnoea. The haemoglobin level was normal or raised. On blood gas analysis, PaO2 and PaCO2 were moderately low, PvO2 was moderately low and PvCO2 very high. 2,3 DPG (diphosphoglycerate) levels were also raised. These findings suggested a defect in oxygen transport and tissue anoxia.

The ICMR report (1985) states that even two months post exposure, nearly 40% of patients attending the hospital presented with respiratory symptoms of breathlessness, cough and in some cases fever. Persistent tachypnoea was a characteristic feature. In some patients, symptoms were out of proportion to clinical and radiological observations.

It has been reported that many of the delayed deaths were preceded by severe respiratory distress.

### 9.2.3 Haematology

Ram Singh (ICMR,1985) reported initial haematological findings, 15 days after the exposure. There was haemoconcentration and leucocytosis. There was no evidence of coagulation disorders. Approximately 25% of severly exposed cases, reporting to hospital, had haemoglobin levels above 14 gm% and 33% had raised eosinophil counts ( above 20% ).

The ICMR report (1985) describes another series of 237 cases investigated during the first two weeks. Polymorphonuclear cells were increased in 35 % of cases, 52% had raised lymphocyte counts, 19% had eosinophilia in excess of 20%, and 15% had haemoglobin levels above 14 gm %.

The ICMR report (1985) quotes a study finding of a 20 - 60 % reduction of the free amino groups in the haemoglobin of persons exposed to the toxic gas.

### 9.2.4 The gastrointestinal system

The ICMR report stated that patients also presented with nausea, vomiting and burning in the stomach. Endoscopic examination revealed superficial gastritis and oesophagitis. A small proportion had hepatomegaly.

### 9.2.5 The neurological system

ICMR reported that immediately after the disaster severly affected cases showed varying grades of loss of consciousness ranging from mild to deep coma. The main presentation in children was coma. They report that in a study of neurological disorders in the affected population , 128 adult subjects were screened and revealed the following :

neuromuscular weakness- 1, right hemiplegia - 1,

hearing loss - 2, tremors and vertigo - 2.

The method of selection and source of cases has not been mentioned, nor whether a standardised method of examination was used.

Andersson et al (1984) reported that those who fell unconscious had few or no eye symptoms or signs on recovery. They also found that collapse and unconsciousness was noted in the cluster second in distance from the factory and not in the others. No quantitative data has been mentioned, to see if the difference is significant. This observation suggests that different patterns of morbidity may occur in different clusters.

Bharucha (ICMR,1985) reported initial observations of coma, tremors and paralysis in some cases soon after the gas leak. No recognizable patterns of neurological disorders were present 5 months post exposure, though many people complained of general weakness.

In the 113 affected people seen at the KEM Hospital Bombay neurological conditions such as sensory motor loss, tremors, loss of consciousness, irritability and depression were found in a significant number of cases.

### 9.2.6 Psychological disorders

Sethi (ICMR,1985), reported that of 168 cases of mental disorders treated in special clinics, the majority were neurotic disorders viz. neurotic depression, anxiety neurosis and hysteria. Psychotic disorders were rare. Women under 45 years were predominantly affected.

S.R.Kamat et al (ICMR,1985) reported on psychometric evaluations carried out on 68 self reporting cases : 22 showed evidence of depression and 19 showed evidence of cognitive defects with poor memory performance.

The team from the National Institute of Mental Health and NeuroSciences (NIMHANS) found a large community load of mental ill health following the disaster (ICMR,1985). They reported that approximately 10 - 12 % of those affected, who visited community based general practice clinics, were presenting with psychiatric manifestations. Symptoms of anxiety and depression were foremost. Sleep disturbances, nightmares, gas phobia, feeling of hopelessness and grief reaction were common. Families of the affected population were finding it difficult to cope with the stressful situation. This is an area needing furthur study, as the NIMHANS team noted that long term after effects have been reported in previous man made disasters.

9.2.7 Outcome of pregnancy

The ICMR report (Mar'1985) reported findings of 97 women who had delivered. Among them there were -

stillbirths - 5 (5.15%)

abortions - 17 (17.5%) ie. total pregnancy wastage of 22.7%

congenital anomalies (minor) - 3

Most babies were full term but with low birth weight, 2kg. on average. In terms of development the babies appeared normal. The mothers weight was 40 - 45 kg.

In the ICMR report (May'85), Dabke described the results of 645 pregnancies : stillbirths - 8

abortions - 67

congenital abnormalies (minor) - 9

low birth weight - 29.8%

They stated that these were not in excess of those expected in a normal population. Rates are calculated by relating the numerator to a given population ie the denominator in a given time period (usually a year). Hence no comments about normality /abnormality can be made from

the above data. Comparison with control groups and if possible with national and regional rates should also be made.

### 9.2.8 The reproductive system

R.Bang and M.Sadgopal (1985) studied the impact on women's reproductive health 2 months post exposure. 55 women were examined in Ob/Gynae field clinics in two of the affected slums - 94% of these had leucorrhoea, 79% pelvic inflammatory disease and 46% had excessive menstrual bleeding. Women also gave a history of suppression of lactation,impotence in the husbands, abortions and stillbirths. This provided a clue that there were adverse effects on reproductive health, particularly womens health, which needed furthur investigation. They admitted limitations of the lack of a control group and small sample size. However there was also the problem of a self selection in clinic based data.

## 9.3 THERAPEUTIC TRIALS

Medical management of patients with eye, lung, CNS, gastrointestinal and other presentations was symptomatic and followed standard practice. This approach did prove life saving and offered some degree of relief to many. However, with the passage of time, it was observed that patients kept coming repeatedly either with persistent symptoms or relapses following a remission.

While it was acknowleged that some of the long term, multisystemic symptoms could be explained as being due to the aftereffects of severe lung damage, ICMR scientists (ICMR,1985) suspected the presence of systemic toxicity. Autopsy findings, laboratory investigations and a rapid literature search lead to the hypothesis of an enhanced cyanogen pool in the body resulting from the

exposure either by direct inhalation of of cyanide or more likely by the breakdown of MIC within the body. The detailed rationale for this has not been reported.

Autopsy findings had shown arterialization of venous blood giving a reddish tinge to internal organs and tissues. Carboxyhaemoglobin and methaemoglobin were not detected. However, samples from all victims showed twin bands of oxyhaemoglobin. It was demonstrated that MIC could produce a reddish colour when mixed with blood.

Urinary thiocyanate levels were found to be higher in the exposed population.

Smoking and/or exposure to smoke, and the eating of certain foods eg cabbage, spinach, cassava etc, are known to enhance the cyanogen pool and result in increased excretion of urinary thiocyanate (which is used as an indicator of cyanide exposure). Rosling (1986) summarised the mechanism of detoxification of cyanide in the body as follows - cyanide is trapped in the erythrocyte fraction of the blood and is converted to the less toxic thiocyanate in the presence of sulfur. This conversion is normally attributed to a reaction with thiosulfate catalysed by the enzyme rhodanase. Thiocyanate is then excreted in the urine. Intravenous administration of sodium thiosulfate is known to increase the capacity for detoxification of cyanide.

The toxic effects of cyanide result from impairment of the mitochondrial respiratory chain by inhibition of the mitochondrial enzyme, cytochrome oxidase. Studies (ICMR,1985) have shown that pure MIC had no effect on cytochrome oxidase, but its degradation products did. This results in under utilisation or non utilisation of oxygen at the cellular level.

Based on the hypothesis of an enhanced cyanogen pool resulting

from the exposure to toxic gases, sodium thiosulfate was administered to some patients as an antidote (ICMR,1985). It was stated that this resulted in marked clinical improvement and a significant increase in PvCO2 in both central and periferal veins indicating better utilisation of oxygen by the tissues.

A double blind study using sodium thiosulfate and glucose was conducted. Of 30 patients, 15 each were given 2 injections of sodium thiosulfate or glucose. Urinary thiocyanate levels were determined at 3 and 5 hourly intervals and compared to the baseline level before the injection. In patients given sodium thiosulfate there was an 8 to 10 fold increase in excretion of thiocyanate in the urine in a significantly large number - in 10 out of 15 patients. Only one of the 15 receiving glucose injections showed such an increase. Criteria for selection into the study have not been stated.

Subsequently, Narayanan (ICMR,1985) reported that of 230 cases treated, complete records were available for 167 ( 87 men, 69 women and 11 children). Symptomatology before commencing treatment was breathlessness and / or general weakness / tiredness. In 29 patients these symptoms were present at rest. While in 132 they were elicited by moderate exercise. Following administration of sodium thiosulfate, 9 showed no improvement while there were varying degrees of improvement in the rest over different periods of time. Details of how the analysis was done has not been stated. There were 10 cases of adverse reactions - 5 with feverishness and one each of skin rash, transient venospasm, a sense of heat over the body, exaggerated reflexes and loss of memory.

On the basis of these studies, a recommendation to use thiosulfate as a therapeutic agent for the victims was made. Indications and contraindications for use, dosages for different age groups and details regarding administration were spelt out.

H.Chandra (ICMR,1985) reporting on the results of sodium thiosulfate in over 2000 cases stated that it was" found to give beneficial results." It is not possible to comment on this. Anecdotal reports of dramatic cures have also been reported.

N.P.Mishra (ICMR,1985) reported on a trial of sodium thiosulfate treatment with 120 cases and 100 suitably matched controls. Only results of clinical observations were recorded as there were no facilities for blood gas analysis. Urinary and serum thiocyanate levels were studied. Urinary thiocyanate levels of controls were in the range of 0.5 to 5.65 mg which is much more than 0.6 to 0.9 mg which has been suggested as the normal range. He therefore doubted the utility of determining urinary thiocyanate levels. He studied clinical findings such as dyspnoea, chest pain, general aches and pains, fatigueability, pain in the abdomen, appetite, pulse rate, lung signs and subjective feelings. All these were given an arbitrary score so that in the worst cases the score totalled to 100. Results showed that in the 100 cases given sodium thiosulfate :

60 showed a decrease in score,

19 had an increase in score and

21 showed no change

The trial was carried out double blind. An important finding was that the greater the initial score before therapy, the smaller was the reduction of the score after therapy. There were very few cases with side effects. These were feverishness, skin rash, sense of heat all over the body - all of which were relieved by antihistaminics. Urinary thiocyanate levels were estimated in 60 cases. The mean value before therapy was 1.068 +/_ 1.03 and after therapy 1.46 +/- 1.113. The basis for selection of cases and controls has not been specified. No comparison between cases and controls has been given regarding

response to sodium thiosulfate administration or regarding urinary thiocyanate levels.

The data reported regarding all the studies done is inadequate for a thorough appraisal.

It is also known that levamisole was used in a few patients as an immunomodulator.

Controlled clinical trials should be performed for treatments being tried, as only then will a scientific evaluation of their efficacy be possible.

## 9.4 DISCUSSION OF CLINICAL FINDINGS

1) From the above account it is apparent that tremendous effort has gone into the clinical management of the thousands of patients who poured into the dispensaries and hospitals following the disaster. Medical staff worked round the clock, many of them suffering from effects of exposure themselves.

2) The description reveals the involvement of several organ systems in the body. This occurred even in the acute phase though it was then masked by the severity of the effects on the eyes and respiratory system.

The Environmental Health Criteria 27 (1983) states that few of the non-biologic agents have unique effects on health and conversely the effects considered may often be related to a wide range of factors. Therefore many aspects of the situation should be takn into account in trying to understan etiology and mechanism of action.

3) Inspite of receiving medical treatment people kept returning to the clinics with histories of persistent symptoms or with relapses following remissions. Recent studies and clinical experience provide evidence of chronic effects.

4) It was not possible to fit the apparantly unrelated symptoms and signs with which people were presenting into definate diagnosis. In the toxic oil syndrome which occurred in Spain clinical observations in the acute and chronic phase showed features resembling those of well known disease entities, but the combined clinical picture and pathology findings were unique and suggested that the syndrome was new (Grandjean and Tarkowski, 1983). A similar situation is seen in Bhopal. Here, unlike in Spain the exposure is much more delineated in time and place. Though the exact composition of the chemicals causing the morbidity and mortality is not fully known, there is certainty about it being MIC and its breakdown products or metabolites. It is the first instance of human exposure to such high concentrationsof these chemicals. The event has resulted in a pattern of morbidity which probably comprises a new disease complex.

5) It has been observed that maintenance of records for individual patients regarding clinical presentation and treatment were a casualty under the acute emergency conditions. This is a lacunae both for the future treatment of the individual patient as well as for a thorough understanding of the pattern of morbidity caused by the disaster.

6) A number of medical professionals and researchers have documented the general clinical picture with which the affected people presented to the clinics at varying periods of time after the disaster. This does provide very valuable qualitative information about the cases seen and investigated.

7) The approach in the documentation reviewed has been focussed mainly on the individual" case" and on specific organs and systems. Some of the limitations of this approach are :

a) Because only people who voluntarily attended clinics were considered there is a self selection in the patients seen and documented. This "selection bias" would result in the picture of

morbidity not being representative of the morbidity in the community. However it would still provide descriptive information about the morbidity produced in those individuals.

From the estimated 200,000 people exposed or at risk only a proportion would have utilised the Govt. health services on which most of the ICMR reports were based. Banerji et al (1985) have documented his. Other possible health services that people may have utilised are as follows :

- medical relief camps set up by a variety of volunatary agencies
- local private practitioners or registered medical practitioners - special health schemes of which they were members eg ESI hospitals, Railway health services etc.
- health services outside Bhopal
- other systems of medicine / healing prevalent in India eg ayurveda, unani, siddha, homepathy etc
- some may have utilised several systems of medicine
- or some may not have utilised any service.

Factors affecting utilisation of services would include accessibility in terms of finance and distance; severity of illness; tolerance of symptoms; mental health status and the beliefs and culture of the people.

b) Cases reported only represent individual patients and cannot be related to a population to derive rates. Morbidity rates besides providing an estimate of the magnitude of the problem and its distribution in the population, could also help one to identify priority groups for treatment and care.

## CHAPTER 10

## REVIEW OF EPIDEMIOLOGICAL STUDIES

### INTRODUCTION

There have been very few epidemiological studies about the health impact of the disaster. Reports that are available have been of studies conducted by non governmental groups. They provide important information about the type and distribution of morbidity in the community. The methodology and findings of these studies will now be described in some detail. Findings from the population based, cross sectional study by Banerji et al have been discussed earlier in the section on mortality.

### REVIEW OF STUDIES

#### 10.1 Epidemiological study of eye and general morbidity

1) Andersson et al (1984) conducted a survey in the first fortnight (Dec 11-17,1984) "to assess possible long term visual disability among survivors". The sample comprised of 8 clusters of households, selected in different localities which had received varying degrees of exposure. Two localities of similar socio economic status, 15 and 17 km away from tha factory, were selected as the control groups.Details of location of the exposed groups are not known. The sample size consisted of 261 exposed and 91 unexposed individuals. The sample size and distribution of the population in each cluster is not known. It was stated that the sample size was restricted because of shortage of time before the exodus from Bhopal during Operation Faith, which disrupted daily life for some weeks. Assumptions to determine sample size have not been mentioned. It was observed that the worst afflicted families had left by the time of the survey leading to an underestimation of effect. Method of sampling has not been mentioned - it was probably not randomly done. Three

ophthalmologists (one with an interpretor) were the interviewers. An attempt to maintain uniformity was made - standard questions, method of examination and simplified nomenclature was used.

Findings :

The post exposure death rate (which was specified as the number of deceased / the number exposed) in the worst affected cluster was 3%. There were differences in symptoms between the various clusters or exposure groups :

- burning of eyes and throat and coughing were the most frequently mentioned symptoms.
- vomiting was the third most frequently mentioned symptom in clusters close to the factory.
- further away choking and shortness of breath was higher.
- collapse and unconsciousness was reported only in the cluster second in distance from the factory. Among those unconscious, there were few or no eye symptoms, upon recovery.
- signs of respiratory distress were most marked in this cluster affecting about 20% of the community.
- over one half of this cluster demonstrated eye signs.
- fundal changes were more common in the exposed group especially venous dilatation.
- there was no case of blindness, irreversible eye damage or difference in age standardised visual acuity.
- there was a significantly higher proportion of people with active eye infection in the unexposed communities ( 5% as compared to 1% ). It was stated that this was possibly due to widespread use of antibiotics in the week preceding the survey. (Absence of secondary infection was observed by Bang in the respiratory system.)

- there was a similar incidence (this should be prevalence ) of Bitot's spots in the exposed and control groups reflecting a similar nutritional status in the 2 groups.

- there was evidence of fairly widespread trachoma in all the groups, though very few active cases were seen.

Andersson et al (1985) reported on a 2 month follow up in the clusters mentioned above. Among the exposed excluding one cluster to which they had "no access " the follow up rate was 50%. In both the exposed and nonexposed groups only 36% (131/360) were located and reexamined. This is a very high drop out rate. No information has been given about the baseline or known characteristics or attempts to follow up the dropouts. The clusters were enlarged and 490 people were examined. No information is given about the new examinees viz. regarding their distribution according to localities, their demographic structure, method used for their selection etc. Hence data will have to be interpreted with caution.

Findings :

There were no cases of blindness, decrease in visual acuity or defect in colour vision. There were no corneal scars in the original group but 6 scars which could impair vision were detected in the new examinees. It was not stated whether these were attributable to the disaster. There was regression of the early healing seen in the first examination. There was one case of persistant unilateral corneal oedema and 3 with complaints of persistent excess watering in an otherwise quiet eye.

## 10.2 Epidemiological study of general health status

A.Patel et al (1985) conducted an epidemiological study of the general health status of the exposed people.

It was a population based, cross sectional study, using an exposed and a control group. The study was conducted 3 months after the disaster. Post exposure mortality rates for the different localities, as given in publications by the State Govt., were taken as indicators of the degree of exposure. JayaPrakash (JP) Nagar, 100 yards from the factory in the direction of the wind that fatal night, had an exposure mortality of 2.34% and was chosen as the study population. Anna Nagar, 10 km from the factory with an exposure mortality of 0.32%, was used as the control group. Both areas were comparable with respect to housing, sanitation and economic status of the population. Study results showed that mortality rates were useful indicators of exposure. However the crude mortality rates found in the study population were much higher than those reported in the Govt. publication. The study findings were:

J.P Nagar - 86.6/1000 population,

AnnaNagar - 7.9/1000 population.

Post disaster hospitalisation rates were also found to indicate differences in exposure : J.P Nagar - 30%

AnnaNagar - 0.72%

Sample size determination was made on the assumption that morbidity would be 15% in JP Nagar and 5% in AnnaNagar. With a 5% level of significance and 90% power, a sample of 180 persons in each group (exposed and control) was chosen. Persons of both sexes, more than 10 years of age were studied.

Numbering of all the households to provide a sampling frame was already done by the ICMR and the same was utilised in this study. As random selection of individuals was not possible, a random selection of 50 household units was made to yield the required sample size.

A house to house survey was conducted. This consisted of the following : a) a detailed history on a predesigned questionnaire.

Non standardisation or pretesting of the questionnaire has been accepted as a limitation, and was reported not to have been done because of shortage of time.

b) general clinical examination of all the systems, the parameters for which had been defined.

c) pulmonary function tests using Morgans electronic spirometer set at BTPS. A trained investigator, with experience in field based studies carried out the tests.

d) estimation of haemoglobin percentage.

e) open ended questions on the people's perception of the health services available after the disaster.

Information about training of the interviewers has not been given. They were not blind to the hypothesis as this was not possible in any of the studies conducted in that situation. Group meetings were conducted in the community to obtain consent. The people were informed about the research group - that they were not related to the Govt., nor were they providers of services, nor involved with the claims for compensation. This would reduce the possibilities for "compensation malingering" as claimed by some. It was found that members of the particular sample chosen had not been included in any of the other studies being conducted, thus ruling out the possibility of the learning effect or Hawthorne effect.

The two populations were comparable with respect to age and sex structure, body surface area, history of chronic disease and smoking. The exposed were slightly better off socio economically than the controls.

There was a rather high non response rate of 29% in the exposed group and 15% in the control group. However available information about the non responders was collected. Their age and sex structure was similar to the responders and 50% or more of them were

exposed. 60% and 50% of non responders in the exposed and control groups respectively were out of town, while 25% were away for work. There were no refusals. Repeated visits were made in the time available to maximise the response rate (the investigators were a group of people who had come from different parts of India and were not resident in Bhopal). It has been argued that since the actual difference in morbidity was much greator than the 10 % assumed in sample size calculations, a smaller sample size would have demonstrated a difference and non response may not make such an impact. Nevertheless the high non response would have altered the process of random selection and it must be kept in mind that the non-responders may differ from the responders with respect to the outcome following the exposure in unknown and variable ways eg as stated by Andersson et al if the more seriously ill were among the non responders there would be an underestimation of effect.

Briefly the study findings are as follows :

Prevalence rates of 26 symptoms were measured in the exposed and control group at the time of the study. Tests to see if the differences were statistically significant were done.

The following 15 symptoms were found to be highly significantly different, being higher in the exposed group : cough with expectoration, breathlessness on usual exertion, chest pain/ tightness, blurred vision/photophobia, fatigueability, weakness in the extremities, muscle ache, headache, tingling/numbness, loss of memory, nausea, abdominal pain, flatulence and anxiety/depression.

The following 6 symptoms were significantly different : dry cough, breathlessness at rest, watering of eyes, skin problems, bleeding tendency and impotence.

The following 5 symptoms were not significantly different :

fever, blood in sputum, jaundice, vomiting,blood in vomit and malaena.

As many as 63% reported all the important symptoms. Only 2.7% reported exclusively pulmonary symptoms, while 35.14% did not report any pulmonary symptoms. Every person in the exposed group reported at least one serious symptom, but quite a few in the control group did not report any.

There was a significant difference in the number of attacks of respiratory infections in the month preceding the study. In the exposed group it was often described as a continuous respiratory problem. It was said that this could be a supportive finding to indicate a state of lowered resistance or immunity.

Exposed women had a significantly higher rate of abnormalities of menstrual flow, alteration in the length of the cycle, dysmenorrhoea and leucorrhoea. The sample was too small to report on abortions and stillbirths. 50% of exposed mothers in the exposed group reported failure of lactation or a decrease in milk output post exposure, compared to 11% in the controls. Impotence in men was reported by 8.1% in the exposed group and 0.7?% in the controls.

On examination:

There was no difference in the resting pulse and respiratory rates. The mean haemoglobin percent in both males and females was significantly higher in the exposed group. There was no case of cyanosis. This was stated to be a significant negative finding in view of the findings of 87% with breathlessness on exertion, the raised haemoglobin concentration and that extensive lung damage was expected to have occurred. 9.4% of the exposed had crepitations and rhonchi in the chest, as against 2.1% in the controls ($P<0.025$). This rate was also stated to be too small to account for the much higher rate of breathlessness on exertion.

**Comparison of Symptoms reported by individuals in J.P. Nagar and Anna Nagar.** (Expressed in percentage. Numbers of cases are shown in brackets.)

| Sl No. | Symptoms | J.P. Nagar % | A. Nagar % | P. Value* (a) |
|---|---|---|---|---|
| 1. | Dry Cough | 27.70 (41) | 14.49 (20) | P < 0.01 |
| 2. | Cough with Expectoration | 47.29 (70) | 23.91 (33) | < 0.001 |
| 3. | Breathlessness at rest | 10.13 (15) | 2.89 (04) | < 0.025 |
| 4. | Breathlessness on usual exertion | 87.16 (129) | 35.50 (49) | << 0.001 |
| 5. | Chest pain/tightness | 50.0 (74) | 26.08 (36) | << 0.001 |
| 6. | Weakness in Extremities | 65.54 (97) | 36.95 (51) | << 0.001 |
| 7. | Fatigue | 81.08 (120) | 39.85 (55) | << 0.001 |
| 8. | Anorexia | 66.21 (98) | 28.26 (39) | << 0.001 |
| 9. | Nausea | 58.10 (86) | 16.66 (23) | << 0.001 |
| 10. | Abdominal pain | 53.37 (79) | 25.39 (35) | << 0.001 |
| 11. | Flatulence | 68.91 (102) | 25.36 (35) | << 0.001 |
| 12. | Lacrimation | 58.78 (87) | 42.62 (58) | << 0. 01 |
| 13. | Blurred vision/photophobia | 77.02 (141) | 33.40 (53) | << 0.001 |
| 14. | Loss of memory for recent events | 45.27 (67) | 11.59 (16) | << 0.001 |
| 15. | Tingling/numbness | 54.72 (81) | 20.28 (28) | << 0.001 |

*(a) P Values were calculated by $X^2$ method.

Source : Patel A and Patel A, (1985)

The Bhopal disaster aftermath :
an epidemiological and sociomedical survey.

**Comparison of Symptoms reported by individuals in J.P.Nagar and Anna Nagar** (Expressed in percentage. Numbers of cases are shown in brackets.) **(Symptoms significantly different but not analysed further)**

| Sl. No. | Symptoms | J. P. Nagar % | A Naga· % | P. Value *(a) |
|---|---|---|---|---|
| 1. | Skin problems | 29.05 (43) | 11.59 (16) | < 0 01 |
| 2. | Bleeding tendency | 9.45 (14) | 2.89 (04) | < 0.025 |
| 3. | Headache | 66.89 (99) | 42.02 (58) | << 0.001 |
| 4. | Muscle ache | 72.97 (108) | 36.23 (50) | << 0.001 |
| 5. | Impotence | 8.10 (12) | 0.72 (01) | < .05 |
| 6. | Anxiety/Depression | 43.92 (65) | 10.14 (14) | << 0.001 |

**Comparison of Symptoms reported by individuals in J.P Nagar and Anna Nagar** (Expressed in percentage. Numbers of cases are shown in brackets.) **(Symptoms - Non-significant)**

| Sl. No. | Symptoms | J. P. Nagar % | A. Nagar % | P. value* (a) |
|---|---|---|---|---|
| 1. | Blood in Sputum | 10.13 (15) | 7.24 (10) | N.S. |
| 2. | Fever | 27.70 (41) | 28.98 (40) | N.S. |
| 3. | Jaundice | 0.67 (01) | 00 | N.S. |
| 4. | Blood in vomit/stool/malena | 12.16 (18) | 10.14 (14) | N.S. |
| 5. | Vomiting | 11.48 (17) | 5.79 (08) | N.S |

*(a) P Values were calculated by $X^2$ method

Source : Patel A and Patel A, (1985)
The Bhopal disaster aftermath :
an epidemiological and sociomedical survey.

There was a statistically significant difference in pulmonary function tests in both sexes in the age groups of 15-45 and 45-60 years. The difference in other age/sex categories were not significant. However there were only a small number of observations in these categories. The mean values of FEV1 and FVC and the FEV1/FVC ratio in all age/sex categories were diminished in JP Nagar compared to AnnaNagar. The 15-45 and 46-60 age groups showed a restrictive pattern while the over 61's had an obstructive pattern.

It was stated that the control population was also minimally exposed, thereby diluting or masking the effect of the exposure.

## 10.3 Epidemiological study of women's reproductive health

R.Bang (19850 conducted a study of the status of women's reproductive health 3 months post exposure. This followed the earlier survey of a small number of women in the 2 affected slums (refer to section on morbidity). The sample consisted of 114 women in 2 severely affected areas and 104 women in a control area. Reasons for selection of sample size have not been given. Selection of the sample was from community based Ob/Gynae clinics. This introduces the problem of self selection as women with Ob/Gynae problems would be expected to attend these clinics. These cases cannot be related to any population or denominator. Hence epidemiological extrapolations from these case studies cannot be made. It is not known if standardised questionnaires or examination schedules were used.

The findings of the study were reported as follows :

| | Exposed group | Control group | Chi square |
|---|---|---|---|
| Total no.studied | 114 | 104 | - |
| Pelvic exam.done | 72 (63%) | 52 (50%) | - |
| Leucorrhoea | 65/72 (90%) | 14/52 (27%) | 51.67 |
| P.I.D. | 57/72 (79%) | 14/52 (27%) | 34.67 |
| Cerv.erosion/ endocervicitis | 54/72 (75%) | 23/52 (44%) | 11.39 |
| Excess menstrual bleeding since exposure | 27/87 (31%) | 1/81 (1.2%) | 26.19 |
| Suppression of lactation | 16/27 (59%) | 2/16 (12%) | 10.17 |

The differences are all highly significant ($P < 0.001$).

The results shown are from a smaller subset of the original sample, as pelvic examination could not be performed in some women due to various reasons like pregnancy; not being married; and refusals ie a selection at this stage has also occurred. However inspite of the limitations mentioned and also because similar factors of self selection occurred for both the exposed and control groups the difference between them is large enough to suggest real differences in the two groups and point to the need to study this area. Other studies, subsequently, too have reported similar findings (Patel et al.,1985 and Sathyamala,1986).

In the exposed group there was a history of spontaneous abortion in 7, stillbirth in 4, threatened abortion in 1 and incomplete abortion in 1 after the gas leak. No women in the control group reported any of these adverse outcomes of pregnancy.

Severe pallor was found in 37 (36%) of the control group but only in 3 (3%) of the exposed group. This corresponds to the finding of an increase in haemoglobin percentage in the exposed population

found in other clinical and epidemiological studies.

10.4 Epidemiological study of outcome of pregnancy

Sathyamala C (1986), conducted a community based study of pregnancy outcome, 10 months post exposure. A large sample was needed to detect significant differences in rates of abortion and stillbirth. The sample size took into account a non response rate of 25% which had been found in earlier studies. A total population of 8165 people in 1632 households were surveyed. Details regarding assumptions to determine sample size, power of study etc were not reported. Three exposed localities (bastis) were selected on the basis of post exposure morbidity and or mortality rate. These were as follows :

JP Nagar- Mortality rate 65.3/1000, Morbidity rate 66%

Kazi camp - " " 46.7/1000, " " 54-60%

Kenchi chola- " " 35.7/1000, " " 91.9%

These figures were taken from later, unpublished analysis of the study by Banerji et al. The sampling frame provided by the ICMR was utilised and random sampling of households done. A" historic control" was utilised ie history of pregnancy outcome in the year preceding the disaster, in the same population was used as a comparison. This was chosen on the basis of studies carried out elsewhere which demonstrated an abortion recall of 82% accuracy even after a lapse of 10 years. This may have lead to an under reporting in the controls and an overestimation of the difference between the groups.

A pre-tested questionnaire was used. Methods used to train interviewers and to avoid interviewer bias have not been mentioned. The definition of abortion, missed periods and delayed periods used for the purposes of the study have not been mentioned. Misclassification between the three could possibly occur

Findings :

The non-response rate was 22 %, within the limits of what had

been considered in sample size determination.

There were 275 live births and 13 still births in the population after the gas leak. The birth rate was stated to be 33.68/1000 population and was said to be comparable with the national birth rate. However births for only 10 months were taken to calculate the rate. Normally a period of 12 months is used and hence the rate calculated would be an underestimation. It is also the crude birth rate, not being standardised for the age and sex structure of the population. The stillbirth rate post exposure was found to be 47.27/1000 live births. However live and still births together should be taken in the denominator. The rate then is 45.25/1000 births. No comparison with national, regional or study based stillbirth rates has been made.

The overall spontaneous abortion rate after the gas leak was 370.96 which was statistically very significantly higher than the spontaneous abortion rate of 32.178 before the gas leak.

Rate of spontaneous abortion before and after the gas leak (GL)

| | Before GL | After GL |
|---|---|---|
| Total conceptions | 404 | 310 |
| No.of abortions | 13 | 115 |
| Abortion rate | 32.178/1000 conceptions | 370.96/1000 conceptions |

A second important finding is that the rate of spontaneous abortions in women who conceived after the gas leak is again statistically highly significantly greater than the abortion rates before the gas leak. The increase being about 5 times greater than before the gas leak.

Abortion rate in conceptions before GL which aborted before GL and abortion rate in conceptions after GL

| Concep. BGL | Abortion BGL | Abortion rate | Concep. AGL | Abortion AGL | Abortion rate |
|---|---|---|---|---|---|
| 404 | 13 | 32.178/1000 conceptions | 310 | 45 | 145.16/1000 conceptions |

(BGL- before gas leak, AGL- after gas leak)

The overall foetal death ratio was statistically significantly increased in the year following the gas leak in comparison to the previous year.

Foetal death ratio before and after gas leak

| Quarter | 1984 | | | 1985 | | |
|---|---|---|---|---|---|---|
| | Number delivered (LB+SB) | Number aborted | F D ratio | Number delivered | Number aborted | F D ratio |
| Jan-March | 30 | 2 | 6.66 | 76 | 27 | 35.52 |
| April-June | 87 | 12 | 13.79 | 77 | 24 | 31.16 |
| July-Sept. | 56 | 3 | 5.35 | 94 | 20 | 21.27 |

(LB - live births, SB - still births;

FD ratio - foetal death ratio )

The foetal death ratio has not been defined but appears to be the number of abortions per 100 live and still births.

While past obstetric history, parity, period of gestation at the time of abortion etc were measured they were not taken into consideration in the analysis. These are important interactive and confounding variables.

Changes in regularity of the menstrual cycle, delayed and missed periods, length of cycle and type of flow, were also found to be statistically significantly different before and after the gas leak.

## 10.5 Case referent study of watering of the eyes

Andersson et al (1986) conducted a case referent study of persistent eye watering. An eye hospital started in Bhopal in response to the disaster was used as the source of cases and controls.

Two consecutive retrospective series of clinical records were drawn, for outpatients on whom exposure data were available. This would be a source of selection bias as it is probable that exposure status may not have been recorded equally in the exposed and non-exposed groups. The method by which exposure was assessed and recorded has not been mentioned.

Findings :

Gas exposed people were three times more likely to present with watering eyes ( odds ratio -OR- 2.96, 95 % confidence interval - CI- 2.3 - 3.4) and nearly 4 times more likely to present with watering and at least one other irritant symptom (burning, itching, redness) ( OR 3.8, 95 % CI 3.12 - 4.4). There was no association between exposure and refractive errors ( OR 1.16, 95 % CI 0.83 - 1.9).

There is no explanation for the symptom of persistent watering of the eyes. The report suggests tear film instability due to long term effect of exposure on epithelial maturation or abnormality of the mucus component of the tear film which is derived from the epithelium itself and from conjunctival goblet cells.

In summary, the epidemiological investigatons conducted have studied different aspects of the health impact of the disaster at different points in time. They vary in methodology used and critical comments regarding this aspect have been given above. They were conducted in difficult circumstances and despite some methodological limitations they all record very serious effects on the health of those exposed. They support clinical findings of multisystemic and long term effects. However some of the important findings from these studies, that may provide clues for etiology, if followed up are -

A) the varying pattern of morbidity in clusters at different distances away from the factory in the acute phase. This was not just in magnitude of effect, but there were qualitative differences of differing symptomatology (Andersson et al) in different clusters. This points to the possibility of the role played by different chemicals. Follow up studies should look at different clusters over time.

B) the presence of a percentage or proportion of individuals with multisystemic symptoms in the absence of lung disease (Patel et al) in the sub-acute phase. This suggests that severe lung damage may not account for all the chronic effects.

C) significantly higher adverse outcome of pregnancy in exposed women conceiving after the disaster, compared to controls. Congenital abnormalities also need to be studied. This very serious observation points to the presence of continuing toxicity.

Infants, preschool and school age children, a vulnerable group have not been studied. Respiratory disability has not been studied at the population level. Natural history of the morbidity and the excess mortality that continues to occur also remain to be studied.

Summary table of epidemiological studies conducted in Bhopal — Methodological aspects

| Investigator | Focus of study | Type of study | Time | Place | Person | Sample size | Sampling method | Non response | Study instrument |
|---|---|---|---|---|---|---|---|---|---|
| 1. Andersson et al | Eyes, gen morbidity | Population based, clusters + controls, + 2 month follow up | December 1984, and Feb. 1985 | Severely + moderately + mildly exposed areas | General population | 261 exposed, 91 un exposed persons | opportunistic sample ie as many as could be examined | 64 % at followup | 3 ophthalmologist interviewers, attempts to maintain uniformity in history taking and examination |
| 2. D Banerji et al | Mortality, general features. | Population based, cross - sectional | January 1985 | Severely + Moderately exposed areas | General population | 700 households | Random sampling | ? | pre-designed questionnaire, trained investigator |
| 3. R Bang | Womens reproductive health | Clinic based case series in exposed + control areas | Feb-Mar 1985 | Severely exposed + control areas | Women-reproductive age group | 114 exposed, 104 un - exposed persons | self selected sample, women attending field based Ob/Gyn clinics | pelvic exam. not done in 43.2% | 1 gynaecologist investigator, routine history taking and clinical exam. |
| 4. A Patel et al | General health | Population based, cross sectional, exposed + control areas | March 1985 | Severely exposed + control areas | General population >10 yrs of age | 180 persons in each group | Random sampling | 29 % in exposed, 15 % in control group | Pre-designed questionnaire with defined parameters, ? training of investigators |
| 5. Sathyamala | Outcome of pregnancy | Population based, cross - sectional, historic control | Sept 1985 | 3severely exposed areas | pregnant women out of general population | 8165 persons in 1632 house-holds | Random sampling | 22 % | Pre-designed, pre-tested questionnaire, ? training ofinvestigators |
| 6. Andersson et al | watering of eyes | case control, record based | Nov'85 -Jan86 | eye hospital | eye patients from gen. pop -ulation | 989 | those with recorded exposure status | - | hospital case records |

# CHAPTER 11

# EXPERIMENTAL STUDIES

## 11.1 Pre- disaster

Data on the toxicology of MIC was scarce at the time of the disaster. Median lethal doses in animals were available eg. it was 5 ppm for 4 hours by inhalation in the rat. In another experiment a dose of 62.5 ppm for 4 hours killed all the exposed rats. Corneal injury has been recorded in rabbits.

A dose ranging study in human volunteers has been referred to by the ACGIH ( American Conference of Governmental Industrial Hygienists). There were no effects at 0.4 ppm but exposure to 21 ppm was unbearable.

Mention has been made of the intense irritation caused to eyes, nose and the throat. Kimmerle and Eben (1964), studying MIC toxicity by inhalation exposure, observed that it was highly irritating to skin and mucosa and that it produced pulmonary oedema.

There was little published material on the effects of sublethal doses, dose response and metabolic/chemical breakdown products of MIC.

## 11.2 Post- disaster

Several toxicological studies on different animal models have been conducted after the disaster. Because of the short life span of the animals used, each animal year being equivalent to several years of human life, an estimate of long term effects of exposure can be made relatively early. Experiments and pathological investigations not ethical or permissable to be conducted on humans can also be performed. The main limitation of animal studies however, in general is that extrapolation of results to humans has to be made with caution because of the differences in the biological systems. Another limiting

factor to be borne in mind in this particular case is that in all the animal experiments conducted so far, only pure MIC has been used as the agent of exposure. In Bhopal under the prevalent conditions of high pressure and temperature and in the presence of catalysts other chemical reactions could have occurred with the formation of other chemicals. However the advantage is that these experiments can indicate lesions attributable to MIC. They can be used to support / explain epidemiological observations and similarly epidemiological data can provide clues for experimental work. The objective of both endeavours together, being to explain mechanisms / pathogenesis to the extent necessary for rational interventions in the treatment and /or rehabilitation of victims and in the prognosis of their condition.

The method of MIC exposure used in animal studies has been by inhalation, with doses varying between experiments. They all tried to simulate the possible dose range that could have existed during the Bhopal disaster

Harding et al (1985) reported the development of lens opacities or cataracts when rat lenses were incubated with MIC.

Salmon et al (1985) reported that at low concentrations in rats MIC caused severe sensory irritation with slow, irregular breathing and the production of a sedative effect. At higher concentrations this was masked by arousal resulting from respiratory distress. Eye damage was always confined to the epithelial layer with most severity at intermediate exposures suggesting that at high doses some protective response was evoked. Urinary thiocyanate levels in the exposed were lower than in the controls. They observed a dose dependant response and supported the use of death rates and incidence of pulmonary damage as a crude index of exposure in epidemiological studies.

Nemery et al (1985) reported that at very high concentrations

(10 mg /L for 15 mins) 50 % of the rats died. The lungs were enlarged with air. Gross oedema or haemorrhage was present only in 2 rats killed after exposure. The main effects of low concentrations of MIC on the respiratory tract was to injure the proximal airways with little alveolar injury. At high concentrations lung parenchyma was also damaged with resulting interstitial and alveolar oedema, inflammation and haemorrhage. Though there was complete destruction of bronchiolar epithelium, repair took place. However despite rapid resolution, they found isolated foci of more recent injury in animals killed 2-3 weeks after exposure. They found MIC to be a respiratory irritant ie both a sensory (stimulation of nerve endings in the nasal mucosa) and pulmonary irritant (impact on lower respiratory tract ).

Ferguson et al (1986) in mice experiments also found MIC to be a potent sensory and pulmonary irritant. They have considerable experience in working with isocyanates and have found MIC to be the most potent pulmonary irritant they have tested in the isocyanate series. They found that the RD 50 (the concentration evoking a 50% decrease in the respiratory rate) and the RD 50 TC (the RD 50 in tracheally cannulated mice) was seperated only by a factor of 1.5. Thus a concentration capable of evoking intense sensory irritation of the eyes ,nose and throat is close to that capable of inducing pulmonary irritation. MIC is thus classified as a respiratory irritant. They found it to be 7 times more potent than chlorine.

Luster et al (1986) found a steep dose response for toxicity. During 90 day recovery studies epithelial injury generally resolved, but prominent fibrosis developed in the walls of the major bronchi. They reported no injury to the spleen, liver, kidney, thymus or brain. Haematological values except for slightly increased haematocrit were within the normal range. They found humoral immunity to be unaffected. Inspite of a 30% suppression in T cell lympho-proliferative response

they found host response resistance not affected.

Fowler and Dodd (1986) studied rats, mice and guinea pigs. Gassert (1986) observed that this study was the most comprehensive inalation study of MIC to date. It was produced some years before the Bhopal disaster under private contract 48 with Union Carbide but was not published until 1986. It provided evidence of bronchiolitis obliterans in guinea pigs (only) exposed to 10.5 and 5.4 ppm MIC for 6 hours. They also noted dose related lesions in the respiratory tract. No deaths occurred in animals exposed to 1 or 2.4 ppm MIC. The majority of deaths for 10.5 and 20.4 ppm occurred through post exposure day 3 ; at 5.4 ppm deaths occurred throughout the 14 days. Deaths were attributed to pulmonary vascular alterations.

ICMR studies (1985) found that the cherry red appearance of the blood could be due to the direct action of MIC (by carbamylatuon) and need not necessarily be due to cyanide or carbon monoxide. Carbon monoxide poisoning was ruled out. Analysis of human tissue by gas chromatography indicated the presence of monomethylamine. On animal studies they found that MIC had an LD 50 dose of 85 mg in mice, but with thiosulfate therapy it shifted to 195 gms. For rats the figures were 270 and 344 respectively. Normal rabbit lungs weighed 6 gms, following MIC exposure they weighed 29 gms and had a large number of haemorrhagic patches. When given sodium thiosulfate immediately after MIC exposure the lungs weighed 24 gms but the appearance was normal. With pure MIC they also found a dose dependant response in the respiratory tract. They found that MIC had bactericidal activity.

Salmon (1986) also reported that MIC could produce a reddish tinge to blood. However differences could be detected on spectrometric analysis.

Varma et al reported adverse effects on the oestrus cycle and fertility in male and female mice

Gassert et al (1986) reported on a 14 month follow up of rats exposed to MIC. Two exposed rats died at 6 and 8 months following sudden onset of respiratory distress. 6 rats killed at 14 months revealed a history of mild respiratory infections. Mild interstitial fibrosis in the peribronchiolar region was present in all exposed rats. A notable finding was that MIC exposed animals had 4 times the amount of lymphoid aggregates found in control animals - adjacent to the bronchiolar airways. A mild infiltrate of eosinophils was present in the bronchiolar mucosa. Eosinophil and lymphoid infiltrates were found in the mucosa of the conjunctiva of the eyelids and perilimbal regions. They state that long term changes in the eyes and lungs may result from a single 2 hour exposure to acute sublethal doses of MIC vapours and that the immune system is most probably directly involved. They suggest that lymphoid hyperplasia may be due to persisting exposure related antigens or to an increased susceptibility to other immunostimulating agents following MIC exposure.

Thus animal experiments reveal that MIC is extremely toxic on inhalation - being a potent respiratory irritant. Chronic morbidity and a continuing increase in mortality has been reported in the exposed animals. The studies suggest 3 possible mechanisms by which this may occur :

a) due to long term sequelae of severe lung damage caused by the direct toxic or irritant effects of the chemicals.

b) due to damage to the immunological system.

c) due to systemic toxicity caused by mechanisms as yet unknown.

# CHAPTER 12

# DISCUSSION

The main points arising from the description so far are summarised. This will be followed by a discussion of the main methodological points pertinent to an epidemiological understanding of the health impact of the disaster. This will also be relevant to the conduct of epidemiological studies in the future. Discussion of methodological issues that have been interspersed in the report will not be repeated here.

## 12.1 SUMMARY OF FINDINGS

1) A population of about 200,000 persons were exposed at a point in time and at a localised place to an airborne toxic chemical agent.

2) The composition and characteristics of the chemical agent/s are not fully known. Studies are being conducted to elucidate this. These include analytical chemical studies, toxicological studies on animals etc.

3) The exposure resulted in immediate and continuing mortality and morbidity in the population at risk.

4) The mortality was substantial, though the exact numbers are not precisely known.

5) Clinical investigations show that the morbidity that has occurred is complex and affects several systems. It does not fit easily into previously known disease entities. The combined clinical and pathological findings probably comprise a new syndrome.

6) Epidemiological studies indicate a large community load of morbidity. This appears to vary with factors like locality, degree of exposure and time. Besides manifestations in the acute and subacute

phases, long term effects have also been observed. Disease occurrence and distribution according to characteristics of person need furthur study.

7) There have been several theories proposed to explain the mechanisms causing the morbidity viz.

- sequelae of direct damage to lung and eyes which followed exposure to the toxic chemicals,
- alteration of the immune system following the exposure,
- systemic toxicity caused by the toxic chemicals or their metabolites in the body,
- psychological trauma caused by the disaster,
- a combination of all the above.

## 12.2 OUTLINE OF DISCUSSION

The discussion on methodological points will cover the following areas : a) the exposure variable,

b) the population at risk,

c) the health outcomes,

d) confounding variables and

e) sources of bias.

## 12.3 THE EXPOSURE VARIABLE

By now, results from the few early studies conducted together with experience of physicians and social workers in Bhopal and toxicological studies in animals indicate that the exposure has resulted in long term adverse effects on health. These findings point to the need for long term follow up of the victims. As a first step valid measurements of exposure need to be evolved.

### a) Defining exposure

It is necessary in the conduct of epidemiological studies in

Bhopal to have a working definition of the exposure variable. Indicators or measures of the degree of exposure are also needed to estimate possible dose dependant responses in the outcome variables of mortality, morbidity and disability.

Previous studies have used the following as indicators of exposure ;

- post exposure mortality rates in defined localities as reported by the State Govt. Study findings have shown that these did provide a rough estimate of exposure in different localities. The rates found in the studies were however much higher than the rates reported by the Govt. Issues concerning mortality rates have been discussed earlier.
- a combination of death in the family or exposure related mortality rates along with grades of morbidity as a measure of exposure.
- one study found that immediate post exposure hospitalisation rates were also related to the degree of exposure.

b) **Variability in exposure**

Epidemiological studies reveal that control areas 10 kms away from the factory have been mildly exposed. Studies have also shown a variability in the picture of morbidity in different localities as well as a variability in individuals or groups of people living in the same locality. Besides differences in individual susceptibility accounting for some of the variability, both the above observations suggest that the factor of "exposure" needs to be considered more carefully. The two important issues to be considered are :

- the area and hence the population exposed may be larger than the accepted 200,000,
- several variables determine the exposure level for an individual. Results from the various studies have indicate that these are :

1) distance from the factory at which the individual was at the

time of the disaster, taking into consideration the direction of the wind,

2) type of housing - pucca (well built)
   - kutcha (without brick and cement)
   - presence of gaps/holes letting in air,

3) action taken at the time of the disaster viz.

   a) measures of exposure to the atmosphere :
      - kept all doors and windows closed and remained indoors
      - opened doors and windows, stayed in the house
      - went out, remained in the area

   b) measures of exertion :
      - left area, walked
      - left area , ran
      - left area, cycled
      - left area , used motorised transport

   c) use of neutralising / protective measures :
      - used a wet cloth over the face
      - covered face with a blanket
      - went in a direction opposite to that of the wind.

Thus a single parameter by itself eg distance away from the factory, may not reflect the true exposure status of the individual which would also depend on other actions that the person took at the time of the disaster. This could be one of the reasons to explain the variability in mortality and in the pattern and degree of morbidity in different individuals even in the same locality. Other factors like age, level of nutrition and general resistance, presence of other diseases etc would also play a role. All the above will have to be considered in studies of morbidity as well as in determining priority groups of people who would need greater care and follow up.

c) **Exposure at individual and population level**

Mortality rates could be a measure of exposure to classify localities and areas ie. they could be used as indicators of degree of exposure at the population level. While the other factors outlined above could be used as measures of the exposure status of individuals.

d) **Measurement (assessment) of exposure**

History taking is the traditional medical method of determining the exposure status of an individual. However in Bhopal a large population has been affected. Several studies into the health effects will need to be conducted over a long period of time and several interviewers will be involved. To ensure comparability between studies and consistency over a period of time, a standard, repeatable and valid method of determination of exposure should be used.A standardised questionnaire, using the factors discussed earlier would provide a simple, inexpensive, noninvasive tool of investigation.

There have been attempts to develop biological markers of exposure eg antibodies or enzyme related markers. They are still in the experimental stage and will have to be field tested. However any invasive method - in this case blood samples will be needed - have the drawback of increased nonresponse. Besides this, increased costs, the need for investigators who have requisite skills, the availability of laboratory facilities etc will have to be considered. Studies carried out so far have shown that the use of crude morbidity and mortality rates have served as markers of degree of exposure. Salmon et al (1985) have confirmed this on the basis of experimental studies. With a little refining as suggested above, standardisation and pretesting, questionnaires could continue to be used to measure the degree of exposure.

## 12.4 THE POPULATION AT RISK

The population at risk would comprise all those who were exposed to the agent and who could potentially manifest adverse health outcomes as a result of the exposure. It would form the denominator in calculating exposure related rates of morbidity and mortality for the population. Various subgroups of this population could also be studied eg according to age, sex, socio-economic status, degree of exposure etc. Epidemiological profiles for groups broadly classified as severly, moderately and mildly exposed could be built up. Factors discussed under exposure variable will have to be considered.

Numbering of all the households to create a sampling framework was done shortly after the disaster. Since a relatively small population has been affected and there is a need for long term follow up, a population register or case registers could be maintained on computer after a census of the exposed population.
This would provide a good base for follow up studies.

## 12.5 THE HEALTH OUTCOME - MORTALITY

### a) Mortality rates / standardization

The number of deaths following the disaster would have to be related to the exposed population to derive crude rates. These could be standardised for age and sex by comparison with a standard population of similar socioeconomic status, and Standardised Mortality Ratios (SMR's) could be calculated. The time period during which deaths are enumerated, would have to be considered in the calculation of exposure related mortality rates. As with morbidity this could be calculated for the acute, subacute and long term phases. Rates for different localities should also be calculated.

These rates could be calculated using routine sources of data.

However in the longitudinal study, life table analysis could be done. There should be a good reporting system for deaths in the exposed and control populations. Staff and investigators should be trained in the use of the International Classification of Diseases and if necessary suitable, standardised criteria could be evolved for the classification of deaths. Autopsies should be performed in a sample of deaths among the exposed group, as is the requirement in any medico legal case.

## 12.6 THE HEALTH OUTCOME - MORBIDITY

a) **Assessment criteria**- This has been the first time that a whole population has been exposed to high concentrations of these chemical agents. The exposure has therefore resulted in a group of symptoms and signs which together do not fit easily into established disease entities. This new disease complex would have to be named appropriately eg the "Bhopal Toxic Gas Syndrome". For the purpose of epidemiological studies working case definitions of this disease complex would have to be developed. This would have to be done based on the clinical experience of medical professionals treating the exposed population together with the help of epidemiologists to ensure simple, standard criteria which can be applied in the field. It would basically comprise of groupings of characteristic symptoms and signs.

b) There may be a **lag period** between the exposure and some pathological conditions which have not as yet manifested. Rothman (1985) states that one must allow for the following

- a biologically appropriate induction time during which a sufficient cause becomes complete. This may be quicker for heavy exposures and slower due to interaction with other factors for lower doses of exposure.
- latent period which is the period after causation before the

disease is detected.

Early studies may thus miss still evolving disease conditions which could be picked up by prospective longitudinal studies or epidemiological monitoring systems.

c) **Complementary causes** or predisposing factors would play a role in the development of the disease outcome by increasing the susceptibility of individuals. People with a larger set of complementary causes would need a smaller dose of exposure to complete a sufficient cause and result in a diseased condition (Rothman 1986). Exposure to the toxic chemicals may unmask or exacerbate existing disease eg chronic bronchitis, asthma, TB etc. These would be considered confounding factors in the analysis of studies. But, from the point of view of the health condition of the people and for the provision of health care services, their presence would cause the individual to be placed in a priority group.

## 12.7 CONFOUNDING AND INTERACTIVE VARIABLES

As discussed previously socioeconomic status is closely related to exposure and to outcome and would be a confounding factor. Stratification in design or group matching could be used to account for this. Age and sex would also have to be considered.

In the Bhopal situation, smoking, exposure to smoke or air pollution in the home (cooking on smoky fires) or at work, nutritional status, presence of chronic diseases eg TB, trachoma, asthma ,chronic bronchitis would be interactive factors which would have to be measured and allowed for in the analysis.

## 12.8 SOURCES OF BIAS

Several sources of bias have to be considered :

a) Stewart (1985) has raised the issue of"**survivor bias**"in follow up

studies of survivors of the atomic bomb explosion in Hiroshima and Nagasaki. This could occur in any cohort of people surviving a major catastrophe. The parent population loses a high proportion of vulnerable individuals - the very young, the old and the sick. Thus when comparisons of mortality are made with a control group in follow up studies there will be an underestimation of the effect. One may get a normal death rate in the survivors, though it may actually be slightly raised. This is similar to the bias caused by the "healthy worker effect" in studies of occupational groups. This factor would have to be kept in mind in long term studies in Bhopal.

b) As discussed previously there would be a **selection bias** in hospital or clinic based studies due to self selection of people attending these services. With the plurality of services and factors of accessibility this would be important in Bhopal.
The utilization of health services in the subacute phase as reported by Banerji et al (1985) shows that this occurs.

c) Bias due to **migration** of people into and out of the population, new births and deaths, all of which would affect the baseline population have been considered earlier in the report.

d) **Misclassification** of exposure status or of outcome (if the diseased condition is undiagnosed or misdiagnosed) will enhance or decrease the association depending on the direction of the misclassification. In Bhopal this is very likely when using routine sources of data, as many medical professionals dealing with a previously unknown situation, have tended to use the nearest known diagnosis to fit the presenting symptoms and signs. This re-emphasises the need to have a working defination of the outcome for documentation and study.

e) The non-response rate has been found to be quite high (20-29%) in all the studies conducted in Bhopal. Besides altering the sample size and the power of the studies, this would also affect the composition of the sample, depending on the characteristics of the non responders. Allowance for non response should be made in determination of sample size and also in budgeting for time and finances to allow for more intensive follow up of a percentage of the non-responders.

f) **Observer bias** leading to a bias in history taking, recording, interpretation of findings or in diagnosis may occur. The factors that play a role specifically in Bhopal are

- Those who believe that all is well in Bhopal try to underplay or explain away the symptoms of the people. This is evident in the attitude of many who attribute every symptom to the presence of chronic diseases or as psychosomatic symptoms or as compensation malingering. On the other hand those who believe that a conscious anti people crime has been committed in Bhopal may let their beliefs affect reporting or interpretation of what the people say.

The above factors could be reduced by the training of interviewers and in the use of blind techniques when possible in certain investigations eg in reading xray films etc. Keeping investigators blind to exposure status is not possible.

g) **Measurement bias** would be important to keep in mind especially when using instrumentation eg spirometers for lung function tests. Standardised instruments and techniques are available. The instruments should be calibrated and maintained to give accurate and reliable readings over a period of time.

## 12.9 SUGGESTIONS FOR EPIDEMIOLOGICAL STUDIES IN BHOPAL

Several research projects, involving different specialities, are being undertaken in Bhopal and elsewhere, on various aspects of the disaster. As outlined earlier there is a need for supportive epidemiological studies, especially those that are population based. I have not attempted to design a specific study while based here in London. More recent information would be available in India, especially regarding the studies set up by ICMR. Also, more details about the affected population, the numbers in different localities, their demographic structure etc would be available in Bhopal. By meeting local medical practitioners and research workers, an assessment of the present status of morbidity could be made, which would provide important clues for study. It is hence more appropriate as well as practical to plan a detailed study design based locally in India, at Bhopal. However, possible study designs and methodological issues concerning longitudinal studies have been delineated.

In Bhopal a cohort of people have been exposed at a point of time to chemical agents. There is a need to study :

1) the range of health effects stemming from the exposure,

2) the natural history of these health effects.

An epidemiological study is basically an exercise in quantifying disease occurence and using a logical method in deriving inferences / explanations to account for variations in disease distribution by relating them to putative causes. In this particular situation, where the exposure has defined time and place characteristics, though the composition may be uncertain, observational follow - up or longitudinal studies seem logical. Here the study population are selected with reference to their exposure status.

The application of case control studies, where the study population are selected with reference to their disease status, would be limited. The disease outcome in Bhopal, is not a well defined entity and is still evolving. The prevalence of what has occurred, is not rare, but affects 30 - 60 % of the severely and moderately exposed population. Also, a large proportion of the local population of similar socioeconomic background have been exposed to the agent, to some degree.

12.9.1 **Cross sectional studies** in the sub acute phase have provided prevalence rates of various symptoms and have also indicated areas of importance. A repeat cross sectional study could give prevalence rates of symptoms and signs 3 years post exposure. It could provide age, sex and area specific distribution of the" Bhopal toxic gas syndrome". Relationships with aspects of the exposure variable could also be tested. Cross-sectional studies using exposed and control groups, a variant of case control studies, could be used for analytical purposes, to study the relationship between symptoms or groups of symptoms and exposure.

12.9.2 Longitudinal study

A cross sectional study should form the baseline for a prospective, longitudinal study. Important points in the conduct of a longitudinal study are now considered .

1) **Objectives**

The hypothesis should be explicitly stated. There is a need to define the time period of the study. This would be selected based on biologic assumptions of the disease outcome and its relationship with the exposure.

The broad objectives could be :

a) to study the prevalence / incidence of the "Bhopal toxic gas syndrome".

b) to relate symptoms / signs observed at the start or appearing during the course of the study, to various aspects of the exposure.

c) to study the natural history of the condition - its severity, fatality, the impact of therapy etc.

Other specific areas to be studied are

- a) the percentage of exposed individuals with multisystemic symptoms and signs in the absence of lung findings.
- b) levels of urinary thiocyanate in the exposed and control population.
- c) prevalence of psychiatric disorders in the two groups.
- d) prevalence of respiratory disabilities
- e) outcome of pregnancy in the years following the disaster.

The specific parameters of these outcomes would have to be evolved locally.

2) **Sample**

Small clusters in different localities could be selected to be able to study the variation in outcome in the different localities. Other aspects of the exposure variable would also have to be measured in the individuals in these clusters.

**Sample size** determination would have to be done locally, with details of the baseline population. Differences in the prevalence of symptomatology between the exposed and control groups, as found in previous studies, should be used for the calculation. The level of statistical significance and power required for the study should be decided. The high non response rate as found in previous studies and possible drop out rates should be considered .

**Method of sampling or sampling procedure** - to ensure

representativeness and to avoid bias, population based, random sampling should be used. With this method the probability of selection into the sample is the same for all individual units. Though the sampling framework has been set up, it could be rechecked keeping in mind the discussion of the population at risk. The method used in the cross-sectional and longitudinal studies would have to be a house to house survey.

Community meetings as in the study by Patel et al should be conducted with the people to inform them of the study, discuss with them the need for continued study, reasons for random sampling etc.

3) **Ethical aspects**

Obtaining consent from study participants and maintenance of confidentiality of patients records should be planned for.

4) **Study population**

Besides the general adult population, infants, preschool and school age children should also be considered. This group has not been studied in the studies reviewed. The advantages of this group are that they would have had no serious exposure to smoke (though passive smoking would have to be considered) and occupational pollutants. Chronic disease would also be minimal.

Their respiratory systems are also more sensitive to insults which makes it easier to detect adverse effects. It has been found that children can carry out spirometric lung function tests from about 7 years and can manage a single measurement of PEFR at 5 years (Florey and Leeder 1982).

5) **Control population**

An unexposed or minimally exposed population is needed for comparison. It should be comparable in terms of broad socio- economic characteristics. It would provide an estimate of disease rates expected to occur in the absence of exposure.

6) **Measuring the exposure and outcome variables**

The main issues regarding these variables have been discussed. Working criteria / case definitions for the assessment of exposure and outcome need to be defined. Several types of outcome can be observed eg post exposure mortality, specified decrease in lung function, onset and frequency of respiratory infections in addition to those mentioned under specific objectives. Sub-classification into definate, probable and ppossible" cases" could be made.

Criteria and methods of assessing the exposure and outcome variables should be the same in both the exposed and control groups.

7) **Examination techniques**

Simple, valid, repeatable, field tested instruments will have to be used. These would include :

questionnaires

clinical examination

lung function tests etc

The parameters to be measured at entry and follow up should be specified. Numerous studies of diseases of the respiratory system and its risk factors have been conducted. Instruments which are valid and reliable are available. Three standard questionnaires have been developed for the study of respiratory epidemiology _ by the British Medical Research Council, U S National Heart and Lung Institute (NHLI) and the American Thoracic Society. A suitable one could be combined with general health questionnaires. Standardised methods for spirometric lung function tests are also available. Random and systematic sources of error in measurment must be minimised.

8) **Other factors** to be considered are

- the training of investigators,
- pilot testing and
- planning for the follow up of a percentage of non-responders.

9) **Analysis**

In a longitudinal study an unbiased estimate of the relation between exposure and outcome is obtained. The relative risk (incidence rate in the exposed/incidence rate in the unexposed) and absolute risk (incidence rate in the exposed - incidence rate in the unexposed) can be calculated. It would be more useful to work out person years of risk and calculate the force of mortality / morbidity or the instantaneous mortality / morbidity rate. The risk of developing a particular outcome (death / disease) can be estimated for a variety of initial characteristics eg distance from factory, action taken at the time of disaster, main presenting symptom in the acute phase etc.

10) **Difficulties**

Drop outs causing attrition of the sample are to be expected. Every effort to get a good follow up should be made.
Substantial loss to follow up may raise doubts the validity of the results as bias would be introduced if the loss is correlated with both exposure and disease.

It is important also to maintain consistent criteria and techniques for measurement throughout the study period. This is in view of the fact that turnover in staff and availability of newer instrumentation and techniques will occur over time.

A longitudinal study is also a major undertaking in terms of resources - personnel, facilities, finances etc. The seriousness of the situation however demand this effort, which would be best conducted under the auspices of the State health authorities and the ICMR.

12.9.3 <u>Multiple or serial cross-sectional studies</u>

Difficulties inherent in the conduct of cohort studies have led to the use of multiple cross sectional studies. This would be

carried out on random samples of the population at different points in time. In Bhopal they would be able to show if there are changes in prevalence from one survey to another. However, since the same individuals would not be followed up, the naturqal history of the disease will not be studied. Changes in population structure in the intervening period could cause a change in the measure of outcome. The sampling method, method of data collection and analysis and response rate should be comparable at each examination. Comparison of mean values or frequencies of variables such as age and sex could give an idea of changes occuring ig the population structure. Sample sizes will be larger than for cohort studies because the greater power of tests of difference between paired observations in the same individual cannot be exploited (Florey and Leeder, 1985). Independent non governmental groups could probably undertake this study design.

### 12.9.4 Epidemiological Monitoring Unit

A detailed longitudinal study with intensive efforts to obtain a good response rate and follow up need be done only for a small sample of the exposed cohort. The setting up of an epidemiological monitoring unit should be considered for the entire exposed population. This would be based on routine records from hospitals and health centres regarding admissions and deaths. It would necessitate the building up of an efficient system of recording, reporting and analysis. A special census of the exposed population could be conducted and a method of identification of exposed individuals evolved. The system would be able to pick up important changes in morbidity or mortality on which appropriate action could be taken.

## CHAPTER 13

## CONCLUSION

The Bhopal disaster has been a human tragedy of immense dimensions. The suffering caused is incalculable. Important tasks remain ahead - for the provision of the best possible care for the victims and for the prevention of such events in the future.

There is a need, first, for the measurement, understanding and documentation of the impact of the disaster on the health of those exposed, so as to be able to provide rational care. It is necessary also to document the seriousness of the effects so as to prevent an easy erasure from human memory of the event. Epidemiologic skills could help in this effort as described in this report.

At the present time it is known that similar small scale "technological disasters" occur frequently. Larger scale disasters could also occur. Hence, along with the deeper causes of these disasters being tackled, there is a need to have a strategy to deal with such events.

Outlines for this are as follows :

- it is necessary to have epidemiological data for an adequate understanding of the effects on human health. This would include data regarding the numbers and demographic structure of the population at risk, the age / sex / area distribution of the fatalities if they occur, and similar data regarding morbidity.
- through collaboration between clinicians and epidemiologists, it would be necessary to evolve simple, standard criteria for assessment and documentation of morbidity.
- similarly, a method to assess exposure needs to be evolved.

- collaboration and communication between administrators, service providers and researchers is important.
- close contact and communication with the affected people is the most important factor. In the absence of this, one could easily slip into esoteric, theoretical exercises, which are meaningless to the problem at hand.

These efforts have to be seen in the context of the broader issues raised by such events. In Bhopal, these would include :

- the economic relationship between multinationals and countries of the Third World which determine factors like technologies and safety systems used,
- the exploitative relationship with the work force and the local community to maintain high profit margins.
- the siting and safety systems of hazardous chemical plants,
- legislation regarding and implementation of safety controls,
- the workers and communities right to information,
- the role of pesticides and
- the acceptable limits to the chemicalization of our world.

The true causes of the disaster and the scope for preventing such events in the future, lie in the matrix of these issues.

## REFERENCES


Adler J and Eldlar R, (1985)
Disaster management - the state of the art, 1984.
Views of an international conference.
Disasters, 9(3),187-189.

Agarwal A and Narain S,1986 (Ed's)
The State of India's Environment 1984-85. The second citizen's report.
"The Bhopal disaster" in the Health chapter.
pp 205-233, Centre for Science and Environment, N Delhi.

American Thoracic Society, (1979)
ATS statement - Snowbird workshop on standardization of spirometry.
Am.Rev.Resp.Dis.,119,831-838.

American Thoracic Society (1985)
(Andrew C et al)
Guidelines as to what constitutes an adverse respiratory health effect, with special reference to epidemiologic studies of air pollution.
Am.Rev.Resp.Dis.,131,666-668.

Andersson N, KerrMuir M, Mehra V,(1984)
Bhopal eye.
Lancet,Dec 22-29,1984, 2:1481

Andersson N et al,(1985)
Bhopal disaster:eye follow up and analytical chemistry.
Lancet,Mar 30,1985,761-762

Andersson N, KerrMuir M, Ajwani M K< Mahashabde S, Salmon A, Vaidyanathan K, (1986)
Persistent eye watering among Bhopal survivors.
Lancet, Nov 15, 1986,1152 (letter)

Anon,(1985)
Recent events point to need for health preparedness for technological disasters.
Disaster preparedness in the America's, Issue No.22,Jan'85

Anon, (abstract),(1985)
Bhopal methyl isocyanate incident - investigation team report.
Union Carbide Corporation, Danbury,Connecticut, 25 pp.

APPEN (Asia Pacific Peoples Environment Network),1985
APPEN Action alert :Bhopal Anniversary, 23,Nov 1985,
Sahabat Alam, Malaysia.

Axford A T et al,(1976)
Accidental exposure to isocyanate fumes in a group of firemen.
Br.J.Ind.Med. 33,65-71,1976.

Aydelotte C L,(1986)
Stepped up inspections, laws mark Bhopals legacy in the U.S.
Occup.Hlth.and Safety, Jan 1986,18-20.

Banerji D and Lakhan Singh,(1985)
Bhopal gas tragedy- an epidemiological and sociological study.
J N U News, April 1985,N Delhi.

Bang A, (1985)
Learning from the relief work- a report from Bhopal.
Medico Friends Circle Bulletin, 109,Jan 1985.

Bang R,(1985)
Effects of the Bhopal disaster on women's health - an epidemic of gynaecological diseases. Part 1 and 2.
Mimeograph.

Baram S M,(1986)
Chemical industry accidents, liability and community right to know.
Am.J.Pub.Hlth. Vol 76(5),568-572.

Baram S M, 1984
Charting the future course for corporate management of health risks.
Am.J.Pub.Hlth. 74(10),1163-1166.

Barker D J P and Rose G, (1984)
Epidemiology in medical practice.
pp 158,Third edition, Churchill Livingston.

Berardinelli P S and Moyer S E,(1987)
Methyl isocyanate liquid and vapour permeation through selected respirator diaphragmsand chemical protective clothing.
Am. Ind.Hyg.Assoc.J. 48(4),324-329,April 1987

Bhargava M P,1985
The Bhopal tragedy - a middle word.
Mimeograph

Bhopal disaster Monitoring Group,(1985)
Bhopal never again.
B.D.M.G. Japan, No. 1, Jan 15,1985.

Bhopal Group for information and Action,(1987)
BHOPAL :Issue's 1,2,3,10,11,Jun'86,Jul'86,Aug'86,April'87,May'87
B G I A, Bhopal, India.

Bhopal Working Group,1987
The public health implications of the Bhopal disaster.
Report to the Program Development Board, Amer.Pub. Hlth.Assoc.
(APHA technical report)
Am.J.Pub.Hlth. 77(2), 230-236, Feb 1987

Bronstein M J,(1984)
The effect of public controversy on occupational health problems: Byssinosis.
Am.J.Pub.Hlth. 74(10),1133 -1137.

Canas R and Kilbourne E M,1987
Oil ingestion and the toxic oil syndrome :results of a survey of residents of the Orcasur neighbourhood in Madrid,Spain.
Int.J.Epid. 16,3-6.

Castleman I B, (1979)
The export of hazardous factories to developing nations.
Int.J.Hlth.Services. 9(4),1979.

Ibid.,(1983)
The double standard in industrial hazards.
Int.J.Hlth.Services. 13(1),1983

Christoffel T and Swartzman D,(1986)
Nuclear Weapons Testing Fallout : Proving causation for exposure injury.
Am.J.Pub.Hlth. 76(3), 290-292.

Diamond S, (1986)
India Carbide trade charges.
New York Times, 20 June 1985, D5.

Diller W, (1986)
Isocyanate effects.
J.Occup.Med. 28(4),265-266, letter.

Documentation for Action Groups in Asia (DAGA)
Asia's struggle to affirm wholeness of life. Report of a consultation on TNC'S in Asia :The aftermath of Bhopal.
DAGA,Hong Kong,Nov 1985

Dodd D E et al,(1986)
Acute inhalation studies with methyl isocyanate vapour - 1.
1) Methodology and LC 50 determinations in guinea pigs, rats and mice.
Fund.Appl.Toxicol. 6(4),747-755.
Ibid. (1986)
2) Respiratory tract changes in guinea pigs, rats and mice
Fund.Appl.Toxicol. 6(4),756-771.

Editorial (1966)
Hazards of disocyanates
Lancet,Jan 1,1966, 32-33.

Editorial (1984).
Calamity at Bhopal.
Lancet, Dec 15

Enright P,(1986)
Spirometer use helps detect lung disease in time for treatment.
Occup.Hlth and Safety. 74-77,April 1986.

Environmental Health Criteria, 27 (1983).
Guidelines on studies in Environmental Epidemiology.
IPCS International Programme on Chemical Safety.
UNEP, Geneva,1983.

Ferguson J S et al (1986)
Sensory and pulmonary irritation with exposure to methyl isocyanate
Toxicol.and Appl.Pharmacol. 82(2), 329-335.

Fienberg S E et al, (1985)
Longitudinal analysis of categorical epidemiological data :
A study of Three Mile Island.
Envir.Hlth.Persp. 63,241-148.

Florey C du V and Leeder S R (1982)
Methods for cohort studies of chronic airflow limitation.
pp 134, WHO Regional Publications, European Series No. 12.

Gassert T, (1986)
Toxicology of methyl isocyanate - a lesson from Bhopal for disaster prevention.
Dissertation for MSc in Occupational Hygiene, LSHTM,
University of London, Sept. 1986.

Gassert T, Mackenzie C, KerrMuir M, Andersson N, Salmon AG, (1986)
Long term pathology of lung, eye, and other organs following acute exposure of rats to methyl isocyanate.
Lancet, Dec 13, 1986, 1403 (letter)

Goldsmith J R et al, (1986).
Pulmonary function screening and monitoring in occupational health.
J.Occup.Med. 28(8), 656-663.

Grandjean P and Tarkowski S (eds), (1983)
Toxic oil syndrome : Mass food poisoning in Spain.
Report on a WHO meeting, pp82,
WHO Regional office for Europe, Copenhagen.

Haastrup P, (1984)
Indoor fatal effects of outdoor toxic gas clouds.
J.Occup.Accidents. 5,279-290.

Harding J J and Rixon C K, (1985)
Lens opacities induced in rat lenses by methyl isocyanate.
Lancet, 30 Mar'85,762.

Higgins M W and Keller J B, (1970)
Predictors of mortality in the adult population of Tecumseh-respiratory symptoms, chronic respiratory disease and ventilatory lung function.
Arch. Environ. Health Vol 21,418-424.

Indian Council of Medical Research, (1985)
Health effects of exposure to toxic gas at Bhopal.
An update on ICMR sponsored researches. 10,Mar,1985.

Ibid (1985)
Minutes of the third meeting of the working group on thiosulfate therapy of the MIC exposed population. 4,April, 1985.

Ibid (1985)
Minutes of the review meeting of ICMR sponsored researches on health effects of exposure to toxic gas at Bhopal.
May 3-4,1985, Bhopal.

Joffe M, (198□)
Biases in research on reproduction and women's work
Int.J.Epid. 14(1),118-123.

Kapila M, (1986)
An epidemiological report on the health consequences of the Lake Nyos disaster. (Volcano)
Mimeograph, Yaounde and Cambridge, Min. of Pub.Hlth. and ODA,UK.

Kimmel C A and Kimmel G L (1986)
Interagency regulatory liaison group workshop on reproductive toxicity risk assessment.
Envir.Hlth.Persp.66, 193-221.

Kimmerle G and Eben, (1964) Abstract
Toxicity of methyl isocyanate and its quantitative determination in the air.
Archiv.Fuer.Toxicologie. 20, 235-241,(German)

Kreiss K, (1986)
Approaches to assessing pulmonary dysfunction and susceptiblity in workers.
J.Occup.Med. 28(8),664-669.

Luster M I et al, (1986)
Immunotoxicity studies on mice exposed to methyl isocyanate.
Toxicol.Appl.Pharmacol.86,140-144.

MacMahon B and Pugh T F,(1970)
Epidemiology - principles and methods.
pp 376, Little Brown and Company.

Mac Sheoin T, (1986)
Bhopal :a bibliography.
Int.J.Hlth.Services. 16(3), 441-468.

Mcdonald A D et al, (1986)
Spontaneous abortion and occupation.
J.Occup.Med. 28(12), 1232-1238.

Mc Farlane A C et al, (1985)
Australian research into the psychological aspects of disasters.
Disasters, 9(1),32-34.

Medico Friend Circle, (1985)
Medical research in Bhopal : the realities and recommendations.

Ibid. (1985)
Medical research in Bhopal - are we forgetting the people?
MFC Bulletin, 109,April 1985.

Merchant J A,(1986)
Preparing for disaster. (editorial)
Am.J.Pub.Hlth. 233-235, Mar'86

Mileti S D et al, (1975)
Human systems in extreme environments :a sociological perspective.
Monograph 21, Institute of Behavioral Science, University of Colorado.

Morehouse W and Subramaniam M A, (1986)
The Bhopal Tragedy : What really happened and what it means for American workers and communities at risk.
A report for the Citizens Commission on Bhopal.
Council on International and Public Affairs, USA

Moyer S E and Berardinelli P S, (1987)
Penetration of methyl isocyanate through organic vapour and acid gas respirator cartridges.
Am.Ind.Hyg.Assoc.J. 48(4), 315-323.

Nagrik Rahat aur Punarvas Committee (Nagrik study)(1985)
Medical survey on Bhopal gas victims.
In association with the Voluntary Health Association of India, Delhi and The Bhopal Relief Trust, Bombay, Mar 1985.

Nemery B et al, (1985)
Effects of methyl isocyanate on the respiratory tract of rats.
Br.J.Ind.Med. 42,799-805.

NIOSH (abstract), (1977)
Organoisocyanates in "Information profiles on potential occupational hazards.", NIOSH contract No. 210-77-0120,
265-275, Oct 1977.

Parnell H A, (1986)
Perspectives in the development of asbestos litigation and its future implications.
Am.Ind.Hyg.Assoc.J. 47(11), 708-711.

Patel A and Patel A, (1985)
The Bhopal disaster aftermath :an epidemiological and socio- medical survey.
Medico Friend Circle, pp, 1985

Peto R et al (1983)
The relevance in adults of air flow obstruction, but not of mucus hypersecretion to mortality from chronic lung disease.- Results from 20 years of prospective observation.
Am.Rev.Resp.Dis., 128, 491-500.

Phoon W O et al (WHO task force), (1986)
Carbamate pesticides : a general introduction.
Environmental Health Criteria 64, pp 137.
International Programme on Chemical Safety (IPCS).
WHO, Geneva.

Rinsky et al, (1986)
A mortality evaluation of employees with potential exposure to MIC.
J.Occup.Med. (letter), 28(3), 243.

Rosling H, (1986)
Cassava, cyanide and epidemic spastic paraparesis- a study in Mozambique on dietary cyanide exposure.
pp 52, Uppsala University, Sweden.

Rothman K J, (1986)
Modern Epidemiology.
pp 358, Little Brown and Company.

Rye A W, (1973)
Human responses to isocyanate exposure.
J.Occup.Med. 15(3), 306-307.

Salmon A G et al, (1985)
Acute toxicity of methyl isocyanate : a preliminary study of the dose response for eye and other effects.
Br.J.Ind.Med. 42, 795-798.

Salmon A G ,(1985)
Does acute toxicity testing tell us anything useful?
Methyl isocyanate as a test case.
Br.J.Ind.Med. 42,577-578

Sangster B and Cohen H, (1985)
Medical aspects of environmental pollution - environmental incidents in the Netherlands 1980- 84.
Clinical. Toxicol. 23 (4-6), 365-380.

Sango C R L and Skarping G, (1986)
Determination of isocyanate and aromatic amine emissions from thermally degraded polyurethanes in foundries.
Am.Ind.Hyg.Ass.J. 47(10), 621-628.

Siesjo B K, (1985)
Oxygen deficiency and brain damage: localization, evolution in time and mechanisms of damage.
Clin.Toxicol. 23(#_$), 267-280.

Simmonds J, (1987)
Europe calculates the health risk.
New Scientist, 23 April, 1987.

Special Supplement (1986)
Health effects of volcanoes : an approach to evaluating the health effects of an environmental hazard.
Am.J.Pub.Hlth., supplement,76, pp 90.

Stewart A, (1985)
Detection of late effects of ionizing radiation : why deaths of A-bomb survivors are so misleading.
Int.J Epid. 14 (1), 52-56.

Tamashiro H et al, (1985)
Mortality and survival for Minamata disease.
Int.J.Epidem. 14(#0, 582-588.

Teague H J (1985)
Cyanide poisoning of Bhopal victims (?) - a hypothesis.
Unpublished article.

Traver G A, Cline MG, and Burrows B, (1979)
Predictors of mortality in chronic obstructive pulmonary disease- a 15 year follow up study
Am.Rev.Resp.Dis., 119, 895-902.

Varadarajar et al (1985)
Report on scientific studies on the factors related to the Bhopal toxic gas leakage.
Council for Scientific and Industrial Research (CSIR), India.
81 pp, Dec 1985

Vincent W J, Ketcham N H, (1980)
A new fluorescence procedure for the determination of MIC in the occupational environment.
Analy.Tech.in Occup.Hlth.Chemistry. ACS symposium series No. 120, 121-147.