EDITORIAL

BHOPAL GAS DISASTER

Twelve years ago, on 2/3rd of December 1984, World's worst chemical industrial disaster occurred at Bhopal as a result of leakage of forty two metric tons of methyl isocyanate (MIC) from the Union Carbide factory (1-3). The leakage had resulted in the immediate death of approximately 2500 people and in the exposure of an estimated population of 200, 000 in the city of Bhopal which had about 800, 000 inhabitants in 1984 (4). Animal experimental studies done to evaluate the short term and long term effects had demonstrated that irreversible multisystem damage could result from MIC toxicity (5-6). However, the exact nature of human health effects can be obtained only from studies carried out in victims at Bhopal. This editorial gives an account of the toxic effects of the gas on human health based on the published reports in the literature.

Mortality:

The maximum number of immediate deaths were recorded in residential areas near the Union Carbide factory, viz. Jaya Prakash Nagar, Kazi camp, Kenchi chola, Chanbad, New Kabbad Khana, Sindhi colony and Railway colony. The maximum mortality was in the 0 to 5 year and above 60 year age groups. Most deaths occurred within 48 to 72 hours of the disaster. Anderson et al in an epidemiological study conducted during the first 10 days after the disaster, found the crude death rate 30 per thousand (7). The Indian Council of Medical Research estimated that the death rate in some of the worst affected areas was 20 per thousand of population in the first 48 hrs (2). For the month of December 1984, the death rate was about 24 per thousand as compared with the national average of one per thousand for a corresponding period (2). Mortality rates declined, but were still slightly higher in the severely exposed areas (8.75/1000) in comparison with the control areas (7.5/1000) during the period May 1989-May 1990 (8).

Autopsy studies:

One common post-mortem presentation was the presence of a thick tenacious foamy froth covering the nose and the mouth. Another common feature was the red conjunctiva. The post mortem hypostasis was not confined to the dependent parts but was present all over the body(2).

The lungs showed congestion, haemorrhage and consolidation; they were enlarged and highly oedematous. The vessels were filled with thick viscid dark cherry red blood. The bronchi and trachea were red in appearance and filled with white tenacious material. The heart often contained blood clot which was cherry red and some chicken fat like material. The liver showed haemorrhagic spots. The gall bladder was distended. Frequently, the stomach and intestines showed haemorrhages in the wall and in the sub-mucosa. The spleen was shrunken and softened. The kidneys showed focal haemarrhages. The brain was cherry red in colour. It was oedematous and softened in consistency. On section, there were foci of haemorrhage, particularly over the white matter. In a few cases, there were sub-arachnoid, intraventricular and intracerebral haemorrhages (2).

MIC trimer was found in the preserved autopsy samples of gas tragedy victims along with dimethyl isocyanurate (DMI), dione and several other unidentified compounds. These constituents were also located in the tank no 610 (from which the toxic gas had leaked) residues, thereby proving that the MIC and its reaction products had passed the lung barrier (9,10).

Histopathological studies:

Although many organs were affected, the most prominent findings were in the lungs. In the early series, there was a gross increase in the weight of the lungs, nearly three times that of the normal. There was intense congestion and denudation of the epithelium of the trachea and the major divisions of the bronchi. There were foci of ulceration. The lungs were heavily water-logged and had the characteristic cherry red colour. Microscopically there were extensive changes such as necrotizing bronchiolitis and widespread damage of the lung parenchyma. The major findings were those of acute bronchiolitis, bronchopneumonia, pulmonary haemorrhages, pulmonary oedema with outpouring of albuminous fluid into the alveoli, pneumonitis and alveolitis. There was extensive cerebral oedema or swelling, and pericapillary ring haemorrhages both in the cortex as well as the white matter. The liver in a number of cases showed varying degrees of fatty change. The kidneys showed marked congestion in most of the cases and tubular necrosis in some. The gastro-intestinal tract showed mesenteric and sub-mucous haemorrhages and necrotizing enteritis. The heart muscle showed generalized oedema without obvious necrosis (2). A subsequent group of autopsies on victims who died during the 8-12 week of the episode revealed less marked but essentially a similar picture of pulmonary changes.

In the middle of 1985, the earlier picture of pulmo-

nary oedema, bronchopneumonia and inflammatory or necrotizing bronchiolitis was gradually replaced by the picture of interstitial pneumonitis but without any significant fibrosis. Bulk of autopsy material obtained in 1986-87, showed the picture of interstitial pneumonitis with thickening and increased cellularity of the alveolar septae progressing to more organised fibrosis as judged by increasing amount of reticulin and collagen fibres. Bronchiolitis obliterans was seen occasionally. There was evidence of desquamative interstitial pneumonitis revealing the alveoli filled with large numbers of macrophages derived from septal histiocytes. Another significant observation during 1986-87 is a picture of chronic passive venous congestion of the liver with characteristic concentration of centrilobular congestion of the liver cell, cords and pigmentary changes. These findings suggest that probably the pulmonary hypertension resulting in right ventricular failure had developed secondary to lung involvement (11).

Electron Microscopic Studies :

Ultrastructural studies of representative samples of tissues at different periods showed a consistent reduction and loss of Type 1 pneumonocytes. By contrast the Type 2 pneumonocytes characterised by the presence of multilayered lamellar concentric bodies representing the precursor of pulmonary surfactant were consistently found. Electron microscopy of the brain confirmed the histological findings of cerebral oedema and neuronal degeneration. Neurones showed depletion of Nissl granules, and marked swelling of pericapillary astrocytes. Flocculent opacities in the mitochondria signifying cellular death were seen quite frequently in sections from the heart muscle, liver cells and nerve cells of the brain (2).

Spectroscopic Analysis of Blood :

Blood samples from cadavers and patients who survived through the gas disaster subjected to spectroscopic and spectrophotometric analyses early in December 1984 did not show the characteristic absorption bands of carboxy-haemoglobin and methaemoglobin. The twin absorption band of oxyhaemoglobin was detected in all the samples tested in this study (2). However, another group of workers have reported an elevated carboxy-haemoglobin and methaemoglobin, which declined after three months (12).

Studies on cyanide toxicity :

Because hydrogen cyanide (HCN) had been implicated in the acute injury from the gas (13), and HCN can be produced when MIC is heated upto 200°C (14), the cyanide levels were estimated in the blood and tissues collected from dead and living gas exposed people during 1985-86 (15). The mean cyanide level in control blood (living) was 20±7.8 ug% and in the blood of gas exposed (living) patients, it was 70±0.22 ug%. The mean cyanide level in control postmortem blood was 25. 0±0.11 ug%, whereas in exposed postmortem blood, it was found to be 150±73.2 ug%. Thus the blood cyanide levels were significantly higher in gas exposed living patients and postmortem blood samples (15). In addition, the urinary excretion of thiocyanate in gas afflicted victims was estimated in comparison with unaffected controls. Studies initiated in December 1984, revealed a three to four fold increase of urinary output of thiocyanate. This was followed by a further enhancement of the urinary thiocyanate levels following intravenous administration of sodium thiosulphate (2).

Double blind tests carried out to assess the response to sodium thiosulphate had revealed that there was a six to eight fold spurt in the excretion of urinary thiocyanate following sodium thiosulphate injection. Marked symptomatic relief and clearing of the thiocyanate levels in the early days of the disaster indicated that the "cyanide pool" of the body might be elevated in the gas victims and could be mopped up by creating an abundant "sulfane" pool by administration of exogenous sodium thiosulfates (2). With the lapse of time there was, however, a decline in the baseline pre-injection levels of urinary thiocyanate and consequently a dcreasing response to the drug(2).

Studies on alterations in haemoglobin :

A significant compensatory elevation of the haemoglobin level in gas afflicted patients was observed. A possible functional impairment of haemoglobin was confirmed by demonstrating that there was a marked three to four fold increase of 2-3 DPG (2-3 Diphosphoglycerate) levels. They were comparable to those obtained in subjects taken to an altitude of 15000 feet and acclimatized there for a fortnight. In a subsequent study two months later, the values had come down from the levels observed in December 1984 although they were still elevated as compared to the levels of the unexposed controls (2).

Several samples of blood collected within 120 days of the episode yielded distinct peaks corresponding to valine methyl hydantoin and valine hydantoin on gas-liquid chromatography employing appropriate controls of carbamylated valine prepared by treating valine with potassium cyanate or methyl isocyanate. The presence of valine methyl hydantoin (VMH) as evidence of methyl carbamylation was also confirmed in post-mortem blood (16). These results provide evidence for structural alterations in the mass of haemoglobin at the time of the gas exposure.

Respiratory effects :

Misra et al (17) reviewed retrospectively charts of patients admitted to the Hamidia Hospital. In 544 patients admitted on the initial day, the main symptoms were breathlessness (99%), cough (95%), throat irritation or choking (46%), chest pain (25%), and hemoptysis (12%). Cyanosis was conspicuous by its absence. Radiological studies of 500 victims (18) done 72 hr after the leakage showed interstitial oedema (41%), alveolar and interstitial oedema (41%), and destructive lesions like cavitation, pneumomediastinum or emphysema (8%). 7.2% had evidence of pre-existing lung disease and 2.2% showed no abnormality.

Vijayan and Kuppurao in a study of 129 symptomatic toxic gas exposed individuals 1-3 months after exposure had demonstrated that pulmonary function measurements such as FVC, FEV1 and FMF 25-75% were significantly lower in toxic gas exposed subjects, and 57 subjects (44.2%) had ventilatory impairment (19). The predominant type of ventilatory defect was combined obstruction and restriction. Of these 57 subjects, 5 (9%) had severe respiratory impairment. An index of severity of exposure was derived retrospectively on the basis of the acute symptoms in the victims themselves or the occurrence of death among their family members. With increasing severity of exposure, there was a tendency for a higher proportion of subjects to have increasing impairment in pulmonary function. Isolated small airway disease was present in 9(7%) subjects. Arterial hypoxemia and ventilatory abnormalities were predominant in severely exposed patients. There was a suggestion that a subgroup of patients had features suggestive of Reactive Airways Dysfunction Syndrome (20).

In 224 symptomatic patients studied 2-5 month after exposure, Bhargava et al had demonstrated that airflow limitation with or without reduction in lung volume was the commonest pulmonary function abnormality (21). Severe hypoxemia was rare and none of the patients showed hypercapnia. The pulmonary function abnormalities were mild to moderate degree. In another study of 903 subjects 2.5-3 months after exposure, Gupta et al (22) found that 164 had abnormal chest X-rays. Of these 164 subjects, 65 were determined to have specific radiological changes occured or aggravated as a result of gas exposure. Of the 65, radiological abnormalities were thought to have occurred in 48 subjects as a result of gas exposure and the remaining 17 subjects showed abnormalities suggestive of old disease which was aggravated (symptoms appearing after exposure) by exposure to the gas. Spirometry were done in 783 subjects from the above sample (23). The results showed that 39% had some form of respiratory impairment. The combined pattern of impairment (obstructive and restrictive disease) had the highest prevalence (22%).

Kamat et al (12, 24) in a study of 113 patients found dyspnoea (97%), cough (98%), chest pain (69%), eye congestion (43%), muscular weakness (32%), abdominal pain (30%) and blind vision (29%) between 7 and 90 days after exposure. Predominant radiographic abnormalities were interstitial deposits-linear (82%), punctate (37%), nodular or micro-nodular (27%) and reticular (27%). Other radiographic abnormalities noticed were cardiomegaly (19%), emphysema-pulmonary hypertension (15%), pleural scars (21%) and consolidation (4%). Pulmonary function showed a predominant restrictive lung disorder. An increase in carboxyhemoglobin and methaemoglobin levels were also noticed. Three months after follow up, there were persistence of dyspnoea (85%), muscular weakness (82%), cough (47%), chest pain (46%), poor memory (32%) and blind vision (16%). The mean FVC and FEV1 changed insignificantly over three months. Sequential measurements of maximal expiratory flow volume for 18 months showed chronic respiratory disability with flow volume reductions due to restrictive lung disease (25).

Vijayan et al studied bronchoalveolar lavages(BAL) using flexible fibreoptic bronchoscope in 36 patients 1-2 1/2 yr after exposure to the 'toxic gas' (26). These patients were categorised into three groups (viz., mild, moderate and severe), depending upon the severity of exposure. There was an increase in cellularity in the lower respiratory tract (alveolitis) of the severely exposed patients (in both smokers and non-smokers), compared to normals. The increase in cellularity in severely exposed non-smokers was due to abnormal accumulation of macrophages, and in severely exposed smokers, to macrophages and neutrophils. Mild and moderately exposed patients did not show significant change in cellularity in lower respiratory tract, compared to normal individuals. There was a trend towards increasing cellularity, as the severity increased and higher numbers of total cells were seen in severely exposed smokers, suggesting that smoking is a risk factor. It appeared, therefore, that subjects severely exposed to the toxic gas at Bhopal might have a subclinical alveolitis characterised by accumulation and possibly activation of macrophages in the lower respiratory tract. Smokers, who were exposed to the gas had in addition, accumulation of neutrophils.

Bronchoalveolar lavage studies were repeated in 20 of the above mentioned 36 patients(27). The interval between the two lavages was 1.4 ± 0.6 years. This study had revealed that the lower respiratory tract inflamma-

Lung India (1996), XIV, No.4 (P. 153-160)

tion had progressed from initial macrophage alveolitis to macrophage-neutrophilic alveolitis. BAL studies in a new group of 24 patients 5.1 ± 1.0 yr after exposure had confirmed chronic inflammation of the lower respiratory tract as evidenced by macrophage-neutrophilic alveolitis in these subjects as well. Clinical, radiographic and pulmonary function abnormalities were persistent in a proportion of subjects in both groups. Fibronectin (FN) levels estimated in BAL fluid of 41 patients had shown that 12 (29.3%) subjects had elevated FN levels and nine of these 12 had radiographic abnormalities. Severely exposed subjects (n=30) had significantly higher BAL fibronectin levels compared to normal subjects and mild/moderately exposed subjects. Repeat FN estimations in BAL samples from 10 patients had revealed that five had abnormally hign FN including three who had high FN on both occasions. The number of patients showing abnormal decline in pulmonary function was higher in patients with elevated FN than in patients with normal FN.

In order to evaluate the relationship between lower respiratory tract inflammation, lung function and severity of exposure, BAL and pulmonary function tests were analysed in 60 patients (28). Total lung inflammatory cells and absolute numbers of macrophages and lymphocytes increased as severity of exposure increased. FEV1/FVC% was also significantly lower as severity of exposure increased. In nonsmokers, BAL neutrophils, both percentage and absolute numbers showed significant negative correlation with FEV1 % predicted. Neutrophil percentage was negatively correlated with FEV1/FVC % . Absolute lymphocytes had significant negative correlations with FVC % predicted. Radiographic abnormalities were associated with decline in FEV1 % predicted. There was a significant increase in lung eosinophils as time passed. These studies suggest that the persisting pulmonary function abnormalities in patients exposed to toxic gas at Bhopal may be due to the consequences of abnormal accumulation of lung inflammatory cells (lymphocytes and neutrophils) and that serious abnormalities of pulmonary function occur in patients who had severe exposure to the gas. There is also a suggestion that the lung damage following toxic gas exposure can be irreversible, as it had been demonstrated that decline in pulmonary function is associated with radiographic abnormalities. The appearance of lung eosinophils as time passed may suggest the possibility of the development of advanced disease and nonresponsiveness to treatment (29, 30).

Open lung biopsies in a few patients 6 to 8 months after the exposure showed thickened alveolar walls, macrophages in the alveoli, some interstitial fibrosis and destructive changes in the terminal bronchioles with exudates in the lumen, a picture suggestive of bronchiolitis obliterans (2). In another study (24), lung biopsy in three patients showed peribronchiolar and perivascular fibrosis, interstitial deposits, bronchiolitis and septal and pleural thickening. Computed tomographic evidence of pulmonary fibrosis was also described in a patient with toxic gas exposure (31).

Eye effects :

Ocular sysmptoms included severe watering of the eyes, photophobia, burning and profuse lid oedema (32). A week after exposure, photophobia was still persisting and a minority had lid oedema. Examinations of the eye showed involvement of the corneal and conjunctival epithelium with redness of the eye, corneal ulceration and lid swelling. Slit lamp examination showed a discrete superficial interpalpebral erosion of the cornea and conjunctiva with the typical whorling pattern of new epithelialization (33). Treatment at the initial stage consisted of saline eyewashes, pupillary dilation and topical antibiotics. In a follow up study on the eyes, on survivors, 9 months after exposure, no case of blindness attributable to gas exposure could be detected among the nearly 20,000 persons attending the Bhopal Eye Hospital (34). However, persistent eye watering and other chronic irritant symptoms like burning, itching and redness were noticed. Three years after exposure, on follow up of exposed and unexposed Bhopal residents, Anderson et al (35) observed an increase risk on eye infections, hyperresponsiveness phenomena (watering, irritation, phlyctens), excess cataracts and resolution of the corneal erosions in exposed persons.

Dwivedi et al (36) studied 232 children admitted to Hamidia Hospital and reported ocular burning (100%), eye swelling (95%), redness (94%), watering of the eyes (89%), ocular pain (76%) and photophobia (44%). 6% had corneal involvement ranging from punctate keratopathy to epithelial denudation. In an analysis of 1140 patients admitted with acute oculo-respiratory symptoms, Raizada and Dwivedi (37) noticed chronic conjunctivitis (14%), refractory changes (35%), and persistent corneal opacities (0.5%). No changes were seen in the iris, lens, vitreous or retina that could be attributed to MIC exposure. In a study of 2280 patients 2 to 3 years after exposure, Khurrum and Ahamed (38) observed chronic conjunctivitis (15%), refractory vision changes (3.5%), deficiency of tear secretion (6.7%) and persistent corneal opacities (9%).

In an ICMR study, eyes of 6317 persons from exposed and 1710 from unexposed control population were examined during May 86 to April 88 (39). 2305 (36.5%) in exposed and 833 (48.2%) in control popula-

tion had no abnormality. The prevalence of corneal opacity was 15.7% in the exposed and 5.2% in the control population. The corneal lesions were superficial. The corneal opacities were opposite pupillary areas and were associated with visual deterioration in 3% in afffected area and in 0.78% in control area. The presence of band shaped opacity in the middle of the cornea had been the pathognomonic feature. Another striking observation was the early age onset of cataract. In the age group of 45-54 years, 91 out of 790 (11.5%) had cataract compared to 1 out of 73 (1.4%) in the control area. In the age group of 54 years and above, the prevalence of cataract was similar in the exposed (419 out of 888, 47.2%) and in the control (32 out of 67, 47.8%) population.

Reproductive health:

In a study of 114 exposed and 104 control subjects, it had been reported (40) that leucorrhoea, pelvic inflammatory disorder, cervical erosion/endovcervicitis, excess menstrual bleeding since exposure and suppression of lactation were significantly high in exposed subjects. Verma (41) showed in an epidemiological survey that pergnancy loss and infant mortality were high in gas exposed women. In a sample of 865 women who lived within one Km of the plant and who were pregnant at the time of the gas leak, 43% of the pregnancies did not result in live births. Of the 486 live births, 14% of babies died within the first 30 days as compared to a death rate of 2.6% to 3% for the previous deliveries in the two years preceding the accident in the same group of women. A high incidence of abortions (24.2%) in the pregnant women exposed to toxic gas was observed as compared to those in the control area (5.6%) (39). Other indices of adverse reproductive outcome such as the rate of still birth and congenital malformations were not found to be different. The perinatal and neonatal mortalities were significantly higher in the affected area (6.9 and 6.1% respectively) as compared to the control area (5.0 and 4.5% respectively (42,43).

In order to study the morphology of human placenta, 134 placentae were studied at full term, premature birth and after medical termination of pregnancy (44). The mean weight of the placenta and foetal weight at full term were found to be lower in the gas exposed groups compared to the controls. Hydropic degeneration in the placentae of women who underwent medical termination of pregnancy was higher in the group exposed to gas, as compared to the controls. In full term deliveries, however, hydropic degeneration did not show any significant difference between the gas exposed and the control groups (44).

Genotoxicity and Immunotoxicity:

Studies (45) were carried out on hospitalized patients and residents of the railway colony at Bhopal to evaluate the immune status, genotoxic effects, and detection of mutagens. Immunological studies conducted in 67 individuals showed that there was an increase in the mean absolute number of T cells and T_H cell population. B cells and T8 cells were within the normal range. Only 18 individuals showed normal response to both T and B cell mitogens. The rest were hyporesponsive to one or both T and/or B cell mitogens. DTH response to the two commonly used recall antigens were not affected. There was a slight increase in serum IgM and IgA levels in exposed subjects whereas IgG levels were comparable to normal. Genotoxic studies comprised evaluation of chromosome aberrations, sister chromatid exchange (SCE) frequencies and studies on sperm morphology and motility. From data analysed in 42 patients, a low responsiveness of lymphocytes to PHA, a considerable delay in their cell cycle and a lowering of the mean SCE/cell to 3.06±1.6 as compared to controls (mean 4.95±1.3) were observed. Some exposed subjects showed chromosomal aberrations of minor nature and the frequencies of such abnormalities were within the normal limits. Sperm morphology, motility and counts were comparable to those of normal subjects (45,46). No mutagens were detected by Ames test in the urine of fifteen subjects. In general, abnormalities were inconsistent and of minor nature except in the case of cell cycle parameters which were distinctly abnormal. However, unless they persist, the implications of their existence and relation in the overall toxic effects of the toxic gas are difficult to assess.

In another chromosomal study, done two and a half months after the gas leak to assess the occurrence of chromosomal aberrations (breaks and gaps) in lymphocytes, showed a significantly increased number of breaks and gaps in the exposed subjects (47). Immune function studies in 300 exposed and 10 non-exposed persons showed no difference in mean immunoglobulin level compared to controls (47). The T-cell population (28%) was found to be less than half that found normally in the Indian population. Significant depression of phagocyte activity of lymphocytes was found as compared to controls. Karol et al (48) found MIC-specific antibodies in guinea pigs injected with MIC as well as in 12 of 144 human survivors.

Psychological effects:

Sethi et al (49) in a study of sixty patients attending 10 specified clinics identified 193 (22.6%) patients of definite psychiatric disorder. The main diagnostic cat-

egories were of neuroses-neurotic depression (37.3%), anxiety state (24.9%), adjustment reaction with prolonged depressive type (19.7%) and adjustment reaction with predominant disturbance of emotions (15.5%). Psychoses were rare. Murthy and Isaac (50) noticed the following four major categories of mental health problems in the Bhopal gas disaster victims.

1. Post-traumatic stress disorder: Anxiety, panic and depression in a large number of people who were well functioning and symptom free before December 3, 1984 and this was due to sudden overwhelming and terrifying emotional stress of the disaster.
2. Pathological grief reaction: These patients suffered intense feelings of depression and grief. They also had marked sleeplessness, suicidal ideation, marked disinterest in routine daily activities and an extremely pessimistic view of the future. This is seen in people who had to face the death of their loved ones.
3. Emotional reactions to physical problems: This was seen in subjects who had visual, respiratory, and other physical complications following the MIC exposure. Emotional reactions of depression, hostility, helplessness and a fear of future were more in patients with greater physical problems.
4. Pre-existing psychiatric problem: These persons showed exaggeration of the persisting symptoms.

Haematological and Biochemical effects:

In a study of 695 MIC exposed subjects 2.5 months after the incident, it had been observed that 78% had haemoglobin greater than 7.4 mmol/1 and a higher total RBC count (51). Polymorphonuclear leucocytosis, lymphocytosis and increased erythrocyte sedimentation rates were seen in 11.9%, 40% and 36.4% patients respectively (52). Liver function tests were normal. Blood ceruloplasmin levels were increased 200% over control values in more than 45% of those tested. Urinary creatinine was signigicantly depressed in approximately 40% of the population examined.

Neuromuscular effects:

Barucha and Barucha (53) studied neurological manifestations in 129 adults and 47 children exposed to toxic gas. Three adults revealed evidence of central nervous system (CNS) involvement in the form of stroke, encephalopathy and cerebellar ataxia each. Persistent peripheral neuromuscular syndromes were observed in ten victims (peripheral neuritis in four, myelopathy and L 5 radiculopathy in one patient each and deafness with or without vertigo in four patients). Among the children affected by the gas leak, coma (lasting for a maximum duration of 24 hours) occurred in 24 victims, convulsions in three children and regression of speech in one. Flaccidity and weakness in the muscles were reported by many children but recorded only in three. Considering the magnitude of the exposure to the toxic gas, the proportion of victims who had recognizable neurological syndromes was low.

The human studies reveal that lungs, in addition to eyes, are the main organs damaged in subjects exposed to toxic gas at Bhopal. As these studies have demonstrated that chronic lung inflammation and fibrosis which are associated with decline in pulmonary function and radiological abnormalities, have occurred in the toxic gas exposed subjects especially in those with severe exposure, there is a possibility that mortality from respiratory failure and corpulmonale may increase in this population. Therefore urgent measures are required to rehabilitate these respiratory cripples and to create adequate facilities to provide quality medicare to these unfortunate victims.

VK Vijayan
Cardio-Pulmonary Medicine
TRC, ICMR, Madras 600 031.

REFERENCES

1. Dhara R.Health effects of the Bhopal gas leak: a review. Epidemiologia e prevenzione n 1992; *52*: 22-31.
2. Indian Council of Medical Research, Health effects of the Bhopal Gas Tragedy. April, 1986; pp 1-16.
3. Council of Scientific and Industrial Research. Report on scientific studies on the factors related to Bhopal toxic gas leakage. December, 1985; pp 41-90.
4. Mehta PS, Metha AS, Mehta SJ and Makhijani AB. Bhopal Tragedy's Health effects: A review of methly isocyanate toxicity. JAMA 1990; *2645*: 2781-2787.
5. Vijayan VK. Methyl isocyanate toxicity : A review of animal experimental studies. I. Short-term effects. Lung India 1996; *14*: 24-29
6. Vijayan VK. Methly isocyanate toxicity: A review of animal experimental studies. 2. Long-term effects: Lung India 1996; 14: 38-41.
7. Anderson N, Muir MK, Salmon AG, Wells CJ, Brown RB, Purnell CJ, Mittal PC and Mehra V.Bhopal Disaster. Eye follow up and analytical chemistry. Lancet 1985; *1*: 761-762.
8. Indian Council of Medical Research, Bhopal Gas Disaster Research Centre, Annual Report, Bhopal 1990.
9. Chandra H, Rao GJ, Saraf AK, Sharma VK, Jadhav RK and Sriramamchari S. GC-MS identification of MIC trimer: a constituent of tank residue in preserved autopsy blood of Bhopal gas victims. Med Sci Law 1991; *3*: 294-298.
10. Chandra H, Saraf AK, Jadhav RK, Rao GJ, Sharma VK, Sriramachari S and Vairamani H. Isolation of an unknown com-

pound from both blood of Bhopal aerosol disaster victims and residue of tank E-610 of Union Carbide India Limited - chemical characterisation of the structure. Med Sci Law 1994; *34*: 106-110.

11. Indian Council of Medical Research, New Delhi and Centre for Visceral Mechanisms, Delhi. The Health Problems of Bhopal Gas Victims: Assessment & Management. December 1989, pp 12.
12. Kamat SR, Patel MS, Kolhatkar VP, Dave AA and Mahashur AA. Sequential respiratory changes in those exposed to the gas at Bhopal. Ind J Med Res 1987, *86* (Suppl): 20-38.
13. Correspondents, India: Long-term effects of MIC. Lancet 1989; *1*: 952.
14. Blake PG and Ijadi - Maghsoodi. Kinetics and mechanism of thermal decomposition of MIC. Int J Chem Kinet 1982; *14*: 945-52.
15. Medico-Legal Institute, Bhopal. ICMR Project No.8. Studies on Clinical and Forensic Toxicology of Bhopal Gas Disaster. Consolidated Report (1st February 1985 to 31 March 1990). pp 1-44.
16. Sriramachari S, Rao GJ, Sharma VK, Jadhav RK, Sharaf AK and Chandra H. GC-NPD and GC-MS analysis of preserved tissue of Bhopal gas disaster: evidence of methyl carbamylation in post-mortem blood. Med Sci Law 1991; *31*: 289-293.
17. Misra NP, Pathak R, Gaur KJBS, Jain SC, Yesikar SS, Manoria PC, Sharma KN, Tripathi BM, Asthana BS, Trivedi HH, Sharma VK, Malhotra Y, Verma A, Bhargava DK and Batni G. Clinical profile of gas leak victims in acute phase after Bhopal episode. Indian J Med Res 1987; *86* (Suppl): 11-19.
18. Sharma PN and Gaur KJBS. Radiological spectrum of lung changes in gas exposed victims. Indian J Med Res 1987; *86* (Suppl): 39-44.
19. Vijayan VK and Kuppurao KV. Early clinical, pulmonary function and blood gas studies in victims of Bhopal Tragedy. Biomedicine 1993; *73*: 36-42.
20. Brooks SM, Weiss MA and Bernstein IL. Reactive airways dysfunction syndrome (RADS): Persistent asthma syndrome after high level irritant exposures. Chest: 1985; *88*: 376-384.
21. Bhargava DK, Verma A, Batni G, Misra NP, Tiwari UC, Vijayan VK and Jain SK. Early observations on lung function studies in symptomatic "gas" exposed population of Bhopal. Indian J Med Res 1987: *86* (Suppl): 1-10.
22. Gupta BN, Rastogi SK, Chandra H, Mathur AK, Mahendra PN, Pangtey BS, Kumar P, Seth RK, Dwivedi RS and Ray PK. Effect of exposure to toxic gas on the population of Bhopal. Part I-Epidemiological, clinical, radiological and behavioural studies. Ind J Exp Biol; 1988; *26*: 149-160.
23. Rastogi SK, Gupta BN, Husain T, Kumar A, Chandra S and Ray PK. Effect of exposure to toxic gas on the population of Bhopal. Part II. Respiratory impairment. Ind J Exp Biol; 1988; *26*: 161-164.
24. Kamat SR, Mahashur AA and Tiwari AKB. Early observations on pulmonary changes and clinical morbidity due to the isocyanate gas leak at Bhopal. J Postgrad Med 1985; *31*:63-72.
25. Patel MH, Kolhatkar VP, Potdar VP, Shekhavat KL, Shah HN, and Kamat SR. Methyl isocyanate survivors of Bhopal. Sequential flow volume loop changes observed in eighteen months' followup. Lung India 1987; *5*: 59-65.
26. Vijayan VK, Pandey VP, Sankaran K, Mehrotra Y, Darbari BS and Misra NP. Bronchoalveolar lavage study in victims of toxic gas leak at Bhopal. Indian J Med Res 1989; *90*: 407-414.
27. Vijayan VK, Sankaran K, Sharma SK and Misra NP. Chronic lung inflammation in victims of Bhopal tragedy. Respir Med 1995; *89*: 105-111.
28. Vijayan VK and Sankaran K. Relationship of lung inflammation with changes in lung function and severity of exposure in victims of Bhopal tragedy. European Respir J 1996; *9*: 1977-82.
29. Watters LC, Schwarz MI, Cherniack RM, Waldron IA, Dunn TL, Stanford RE and King TE. Idiopathic pulmonary fibrosis: Pretreatment bronchoalveolar lavage cellular constituents and their relationship with lung histopathology and clinical response to therapy. Am Rev Respir Dis 1987; *135*: 696-704.
30. Boomars KA, Wagenaar SS, Mulder PGH, Van Velzen-Blad H and Van Den Bosch JMM. Relationship between cells obtained by bronchoalveolar lavage and survival in idiopathic pulmonary fibrosis. Thorax 1995; *50*: 1087-1092.
31. Sharma S, Narayanan PS, Sriramachari S, Vijayan VK, Kamat SR and Chandra H. Objective thoracic CT scan findings in a Bhopal gas disaster victim. Respir Med 1991; *85*: 539-541.
32. Anderson N, Kerr Muir M, Mehra V and Salmon AG. Exposure and response to methyl isocyanate: results of community-based survey in Bhopal. Br J Indust Med 1988; *45*: 469-475.
33. Anderson N, Kerr Muir M and Mehra V. Bhopal eye. Lancet 1984; *2*: 1481.
34. Anderson N, Kerr Muir M. Ajwani MK, Mahashabde S, Salmon A and Vaidyanathan K. Peristent eye watering among Bhopal survivors. Lancet 1986; *2*: 1152.
35. Anderson N, Ajwani MK, Mahashabde S, Tiwari MK, Kerr Muir M, Mehra V, Ashiru K and Mackenzie CD. Delayed eye and other consequences from exposure to methyl isocyanate: 93% follow up of exposed and unexposed cohorts in Bhopal. Br J Indust Med 1990; *47*: 553-558.
36. Dwivedi PC, Raizada JK, Saini VK and Mittal PC. Ocular lesions following methyl isocyanate contamination: The Bhopal experience. Arch Opthalmol 1985; *103*: 1627.
37. Raizada SK and Dwivedi PC. Chronic ocular lesions in Bhopal gas tragedy. Ind J Ophthalmol 1987; 35: 453-455.
38. Khurrum MA and Ahmad SH. Long-term follow up of ocular lesions of methyl isocyanate gas disaster in Bhopal. Ind J Opthalmol 1987; *35*: 136-137.
39. Indian Council of Medical Research, New Delhi. Health effects of exposure to toxic gas at Bhopal 1988; 1-26.
40. Narayan T. Health impact of Bhopal Disaster. An epidemiological perspective. Economic and Political Weekly 1990; *35*: 1905-1914.
41. Verma DR. Epidemiological and expreimental studies on the effects of methly isocyanate on the course of pregnancy. Environ Health Perspect 1987; *72*: 153-157.
42. Bhandari NR, Syal AK, Kambo I, Nair A, Beohar V, Saxena NC, Dabke AT, Agarwal SS and Saxena BN. Pregnancy outcome in women exposed to toxic gas at Bhopal. Ind J Med Res 1990; *92*: 28-33.

43. Bajaj JS, Misra A, Rajalakshmi M and Madan R. Environmental release of chemical and reproductive ecology. Environ Health Prospect 1993; *101*: 125-30.

44. Kanhere S, Darbari BS and Shrivastava AK. Morophological study of placentae of expectant mothers exposed to gas leak at Bhopal. Indian J Med Res 1987; *86* (Suppl); 77-82.

45. Deo MG, Gangal S, Bhisey AN, Somasundaram R, Balsara B, Gulwani B, Darbari BS, Bhide S and Maru GB. Immunological, mutagenic and genotoxic investigations in gas exposed population of Bhopal. Ind J Med Res 1987; *86*(Suppl): 63-76.

46. Daniel CS, Singh AK, Siddique P, Mathur BBL, Das SK and Agarwal SS. Preliminary report on the spermatogenic function of male subjects exposed to gas at Bhopal. Indian J med Res 1987; *86*(Suppl): 83-86.

47. Saxena AK, Singh KP, Nagle SL, Gupta BN, Ray PK, Srivastav RK, Tiwari SP and Singh R. Effect of exposure to toxic gas on the population of Bhopal. Part IV. Immunological and chromosomol studies. Ind J Exp Biol 1988; *26*: 173-176.

48. Karol MH, Taskar S, Gangal S, Rubanoff BF and Kamat SR. The antibody response to methyl isocyanate: Experimental and clinical findings. Environ Health Perspect 1987; *72*: 169-75.

49. Sethi BB, Sharma M, Trivedi JK and Singh H. Psychiatric morbidity in patients attending clinics in gas affected areas in Bhopal. Ind J Med Res 1987; *86*(Suppl): 45-50.

50. Murthy RS and Isaac MK. Mental health needs of Bhopal disaster victims and training of medical officers in mental health aspects. Ind J Med Res 1987; *86*(Suppl): 51-58.

51. Srivastava BC, Gupta BN and Athar M. Effects of exposure to toxic gas on the population of Bhopal III. Assessement to toxic manifestations in humans. Indian J Exp Biol 1988; *26*: 165-172.

52. Naik SR, Acharya VN and Balerao RA. Medical Survey of methyl isocyanate gas affected population of Bhopal. J Postgrad Med 1986; *32*: 175-184.

53. Barucha FP and Barucha NC. Neurological manifestations among those exposed to toxic gas at Bhopal. Ind J Med Res 1987; *86*(Suppl): 59-62.