scientific method. We believe doctors who wish to learn from Bhopal are waiting for ICMR doctors to report in peer-reviewed medical journals, all they have learned about MIC and the Bhopal gas tragedy.


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Response:

It must be clarified that the paper based on our scientific studies does not represent any ICMR report. Apart from salient points, details of each study were not included due to space constraints. Data in the Current Science paper were periodically reviewed by the PACs, under the aegis of BGDR (ICMR), presented in several national/international conferences and also published. This work under the exigencies of a disaster was aimed at time-bound solutions to pressing issues of clinical toxicology. Only experimental studies and DBCTs were according to planned protocols, details of which are available in published literature, as well as a thesis.

It is amusing that while criticizing us for relying on unpublished data, the critics themselves have used similar 'unpublished report(s) of CSIR' to contradict cyanogenesis.

MIC and cyanide toxicity

We have been advocating dual toxicity due to MIC and HCN and not cyanide alone. While a single exposure to HCN does not produce chronicity, one exposure to 'acrylonitrile', an organonitrile, required prolonged treatment with a NaTS. Hence, far from 'weaving any imaginary theory of acute and ongoing cyanide toxicity', we were guided by scientific principles of clinico-pathological observation, toxicological evidence and conclusions aimed at prompt clinical relief. In retrospect, NaTS therapy appears to be the single major successful interventional agent in Bhopal compared with other modes such as Levimisol, steroids, bronchodilators, etc.

Acute deaths and autopsies

Late Heeresh Chandra, an eminent and seasoned forensic scientist, strongly believed that the very high mortality rate on the first day of the tragedy was unlikely to be solely due to MIC, which found support in UCC's reports on 85 non-fatel accidental exposures to MIC. History of convulsions and consistent autopsy findings of generalized pinkish hypostasis of the body and cherry red colouration of blood and viscera in victims, favoured cyanide toxicity in accordance with standard textbooks of forensic medicine variations notwithstanding.

Issues of chronic or delayed cyanide toxicity

Instead of primary release of HCN, we proposed the following alternate mechanisms for 'chronic cyanide toxicity':

- Protracted cyanogenesis due to inhaled organonitriles(s) from amongst the eleven unidentified compounds of the tank residue.
- Our initial observations on N-Carbamoylation of Hb led to worldwide speculations on in vivo cyanogenesis. Some reactions, however, may not extend beyond 120-day life span of erythrocytes and turnover of tissue proteins. The demonstration of S-Carbamoylation of glutathione, 30–40% reduction of GSH observed in Bhopal victims and impaired detoxification of endogenous cyanide due to blocking of any of the three cysteinyl residues within the entrapment pocket of rhodanese, led us to propose a pivotal role of reversible S-Carbamoylation in the transport of MIC within the tissues.
- Possibly several other non-enzymatic and enzymatic mechanisms might have an in vivo role in neo-cyanogenesis via 'MIC-bound glutathione'.

Blood cyanide levels

The correspondents have wrongly assumed that all these were autopsy cases, although table 5 clearly indicates that as many as 15 and 34 subjects were live. The controls were drawn from unaffected areas of Bhopal, while subjects were from exposed areas. The samples collected in 1985–86 were cryo-preserved with added NaF and analysed subsequently.

Treatment with NaTS

As early as 8 December 1984, Daunerger reported 2-ppm cyanide levels in the blood of dead victims. Ever since, prompt 'clinical and therapeutic response' to NaTS was recognized. Elevated urinary thiocyanate in autopsy samples and in several series of clinically ill patients provided objective proof. The first DBCT conducted under the supervision of K. Ramachandran confirmed the hypotheses.

Immediately thereafter, Bang et al. under the banner of nfc stated:

Delayed deaths and autopsies

The correspondents seem to be unaware of the Bhopal scenario. After majority of deaths in the first few days, there was a rapid decline in the mortality. Their statement 'How they were selected... amongst many thousands who died' is puerile and they should realize that autopsies are not made to order, much less demographic exposure grading! All autopsies were done as when the cases turned up.
‘In spite of clear evidence of cyanide poisoning from 3 December 1984, the administration of the known specific antidote sodium thiosulfate was banned.’

Again in April 1985, mfc emphatically urged the need to administer NaTS in all symptomatic cases.

Up to early 1986 there was intermittent clinical recurrence, moderate SCN elevation and continued response to NaTS. Later, faced with ‘declining trends’, the majority of members of the Supreme Court Committee recommended cessation of NaTS therapy, when the need no longer existed.

The statement ‘at this point of time that doctors have not been using NaTS for last 20 years’, is fallacious.

Issue of gas release

The incontrovertible evidence of raised blood levels of cyanide and its detoxification product SCN in the urine of victims, constituted the central theme of the Current Science paper. Hence, details of our studies on the presence of HCN in the tank 610-E were not included in it.

In the CSIR report cited by the correspondents, studies were conducted on MIC samples from unaffected UCC tank-611, synthesized by a lab-X and a commercial source. The experiments carried out in Pyrex tubes under different conditions, in no way mimic the reactions that might have occurred in UCC steel tank 610-E.

Instead, our team has successfully demonstrated direct presence of HCN in the residue of tank 610-E, by five different methods, including pyridine-benzidine as well as para-phenylene diamine methods, and observed 500 ng% HCN after aqueous elution. Graded pyrolysis of composite tank residue even at 300–400°C yielded 0.03 to 0.91% HCN. While the temperature attained in tank 610-E is a matter of conjecture, demonstration of HCN in tank residue at ambient temperature, even after a lapse of five years, is ‘direct evidence of release of HCN’ in Bhopal. Hence the correspondents’ assumptions are untenable.

Experimental studies

The so-called serious questions should be set at rest by references 4, 5 hailed by reviewers as ‘fundamental contributions to inhalation toxicology’. The study designs are available in these papers. The references 6, 7 cited by the correspondents describe the results of experimental studies conducted with cold MIC, which is not as toxic as pyrolysed MIC. Hence the conclusion drawn from such studies may not help in understanding the events at Bhopal. In fact, Bucher stated that:

‘Before one can directly apply these results to exposed population in Bhopal, it should be kept in mind that while MIC was probably the primary chemical released during the accident, an as yet undetermined amount of reaction products was also released, perhaps including hydrogen cyanide’.

It can be concluded that the correspondents with pre-conceived notions, have tried to weave a criticism based on some unpublished and some irrelevant published papers to ridicule the cyanide hypothesis. On the contrary, our scientific findings of elevated blood cyanide and urinary SCN levels and response to NaTS therapy, up to 1986, as reported in Current Science, provide convincing evidence. No doubt, the underlying mechanisms discussed above may need reappraisal by the global scientific community.


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