Research

Diethylene glycol poisoning in Gurgaon, India, 1998

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Objective To discover the cause of acute renal failure in 36 children aged 2 months to 6 years who were admitted to two hospitals in Delhi between 1 April and 9 June 1998.
Methods Data were collected from hospital records, parents and doctors of the patients, and district health officials. Further information was obtained from house visits and community surveys; blood and stool samples were collected from other ill children, healthy family members and community contacts. Samples of drinking-water and water from a tube-well were tested for coliform organisms.
Findings Most of the children (26/36) were from the Gurgaon district in Haryana or had visited Gurgaon town for treatment of a minor illness. Acute renal failure developed after an episode of acute febrile illness with or without watery diarrhoea or mild respiratory symptoms for which the children had been treated with unknown medicines by private medical practitioners. On admission to hospital the children were not dehydrated. Median blood urea concentration was 150 mg/dl (range 79–311 mg/dl) and median serum creatinine concentration was 5.6 mg/dl (range 2.6–10.8 mg/dl). Kidney biopsy showed acute tubular necrosis. Thirty-three children were known to have died despite being treated with peritoneal dialysis and supportive therapy.
Conclusion Cough expectorant manufactured by a company in Gurgaon was found to be contaminated with diethylene glycol (17.5% v/v), but a sample of acetaminophen manufactured by the same company tested negative for contamination when gas-liquid chromatography was used. Thus, poisoning with diethylene glycol seems to be the cause of acute renal failure in these children.

Keywords: ethylene gycols, toxicity, poisoning; drug contamination; expectorants, toxicity; antitussive agents, toxicity; kidney failure, acute; child, preschool; infant; India.

Mots clés: éthylène glycols, intoxication; contamination médicamenteuse; expectorants, toxicité; antitussifs, toxicité; insuffisance rénale aiguë; enfant d'âge préscolaire; nourrisson; Inde.

Palabras clave: glicoles de etileno, toxicidad, envenenamiento; contaminación de medicamentos; expectorantes, toxicidad; agentes antitusivos, toxicidad; insuficiencia renal aguda; infante; lactante; India.

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Introduction

The Federal Food, Drug and Cosmetic Act was passed by the United States Congress in 1938 in reaction to a public health accident that occurred in 1937 when 105 people died from diethylene glycol poisoning. Diethylene glycol, a highly toxic organic solvent that causes acute renal failure and death when ingested, was used as a diluent in sulfanilamide, the first sulfa antimicrobial drug (*1, 2*). The legislation,

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which was the first to require that new drugs be tested for toxicity before being put on the market, protected the American public against a recurrence of the tragedy. However, despite the existence of similar, appropriate legislation in India, 14 patients died in Bombay (now Mumbai) in 1986 when they were given glycerine contaminated with diethylene glycol (*3*). We report a second episode of poisoning occurring in 1998 in India as a result of children ingesting diethylene glycol; at least 33 children are known to have died.

Background

Kalawati Saran Children's Hospital is a tertiary level paediatric hospital in Delhi. About 150 cases of acute renal failure were seen in the hospital over the last five years. Paediatricians were able to determine the etiology in most of the cases, but were unable to do so for a large number of children who were admitted from April 1998. Most of these children died. All of these children became ill initially with an acute febrile illness with or without mild respiratory or gastrointestinal symptoms (such as diarrhoea or vomiting, or both). All of the children had been treated by private medical practitioners (qualified as well as unqualified) and had some unknown medicines administered, orally or as injections. After a few days of private treatment, the patients developed severe oliguria or anuria that necessitated admission to the children's hospital. On 5 May 1998 the hospital informed the National Institute of Communicable Diseases about these cases. This triggered an epidemiological investigation to discover the cause. The results are presented in this report.

Materials and methods

The Director of Health Services and the Municipal Health Officer of Delhi were informed about the large number of children with unexplained acute renal failure who had been admitted to the Kalawati Saran Children's Hospital. They were asked to determine whether other hospitals in Delhi had seen similar cases. They found that similar cases had been seen by two other hospitals on or after 19 April 1998: two cases had been admitted to Safdarjang Hospital and 9 to the All India Institute of Medical Sciences. For this investigation, a case was defined as a patient admitted to hospital in April 1998 or later and diagnosed as having unexplained acute renal failure. The 9 cases admitted to the All India Institute have been excluded from this report for administrative reasons. Nevertheless, the excluded cases had epidemiological and clinical characteristics similar to those of the cases admitted to the other two hospitals.

The hospital records of all patients who met the definition of a case were examined to determine the patient's age, sex, place of residence, date of onset of illness, signs and symptoms, results of laboratory investigations, and treatment received before and after hospitalization. Parents of many of the children and the doctors who had treated them were also interviewed. It became apparent that most of the children who had had unexplained acute renal failure came either from the Gurgaon district or had gone there for treatment of acute febrile illness or diarrhoea.

Health officials in the Gurgaon district were contacted to find out whether similar cases had been admitted to the district hospital or to private hospitals in the district. Data were also collected on cases of pyrexia of unknown origin and diarrhoea that had been treated at the district hospital during 1997 and 1998.

Researchers visited the houses of many of the children who had died before the epidemiological investigations began or who were still hospitalized, to discover whether there were any common factors and to discover how these children might have differed from other children in the neighbourhood. These visits were combined with house-to-house surveys of the surrounding community to enquire about any cases of acute febrile illness, diarrhoea or severe oliguria that had occurred since April. Enquiries were also made about the doctors who had treated the children and the types (or names) of medicine prescribed. Blood and stool samples were collected from children who had any illness during these visits as well as from apparently healthy family members and community contacts. Two samples of drinking-water (stored in covered cement tanks) were collected from the houses of children who had had unexplained renal failure. Two samples of running water from a tube-well in a nearby village were also collected. These water samples were tested for coliform organisms.

The treatment histories of the children showed that a large proportion of them had been treated by a local doctor for minor ailments before being referred to the specialized hospitals in Delhi with severe oliguria or anuria. The local doctor was interviewed to provide data on clinical features and treatment of these children. Many other qualified and unqualified doctors practising in Gurgaon were also interviewed.

Blood samples from cases and contacts were collected in plain vials as well as blood culture bottles using aseptic precautions. The samples collected in plain vials were used for serological testing and isolation of viruses. Stool samples were collected in viral transport medium (Hanks balanced salt solution) as well as Cary Blair medium. The samples taken for virus isolation were transported to the laboratories of the National Institute of Communicable Diseases, Delhi, at 2–8 °C and then stored at –20 °C until tested; samples for culturing bacteria were transported at room temperature and processed on the same day.

Stool samples were subjected to virus isolation in various cell lines (RD, HEp2, Vero) by standard procedures. The vials were observed for 7 days. All cytopathogenic agents isolated were subjected to enterovirus typing by a microneutralization test using

pooled antisera procured from the National Institute for Public Health and Environmental Protection (RIVM, the Netherlands).

Representative serum samples were tested for antibodies against group B coxsackievirus by microneutralization test, antibodies against Hantaviruses by particle agglutination kit (Korean Green Cross Corporation, Seoul, Republic of Korea), and antibodies against dengue virus (IgM and IgG) by MAC ELISA using commercial kits. Some samples were also tested for haemagglutination inhibition antibodies against respiratory viruses (influenza A and B, respiratory syncytial virus, and adenoviruses) using HA antigen procured from the Centers for Disease Control and Prevention, Atlanta, GA, USA, and IgM antibodies against cytomegalovirus by micro ELISA (Sigma Diagnostics, St Louis, MO, USA).

Some formulations of medicines manufactured by companies in Gurgaon and two surrounding districts (Faridabad and Bahadurgarh) were collected by the Joint Drugs Controller of India and tested at the Central Drugs Laboratory, Calcutta, for evidence of contamination.

Results

A total of 36 children with unexplained acute renal failure were admitted to two hospitals in Delhi between 1 April and 9 June 1998. Thirty-three of the children are known to have died in hospital or at home after being discharged against medical advice. Only two patients were discharged after improving. The status of one patient who was discharged in critical condition is not known. The progression of the epidemic is shown in Fig. 1.

Table 1 shows the age and sex of the children. They ranged in age from 2 months to 6 years; almost three-fourths (26/36) of cases and three-fourths of the deaths (24/33) occurred among children younger than 2 years. Boys accounted for about 69% (25/36) of cases and 70% (23/33) of deaths. The age-specific and sex-specific case fatality rates were not significantly different.

The episode was centred in the Gurgaon district, Haryana state, and adjoining areas. At the time of hospitalization 64% (23/36) of the children were known to live in the Gurgaon district; of these, 9 lived in Gurgaon town (the main town in the district) and the remaining children lived in distant villages. Three children came from the Rewari district in Haryana; one from the Faridabad district, also in Haryana; and two came from the Alwar district in Rajasthan. At the time of admission, the remaining 7 (19%) children were thought to be residents of Delhi. However, it was later discovered that at least 3 of them were actually residents of the Gurgaon district and that they had given addresses of relatives in Delhi at the time of admission; 2 had become ill while staying with relatives in Gurgaon. All the villages or urban areas reported only single cases.

Field visits to the villages and urban areas where patients lived revealed that a few other cases of fever and diarrhoea had occurred in the neighbourhood, and there had been no increase in such cases. No other case of unexplained acute renal failure or death from anuria or severe oliguria was identified.

Table 2 shows the number of cases of pyrexia of unknown origin and diarrhoea treated in the district hospital in Gurgaon between January 1997 and April 1998. There was no increase in the number of cases of fever or diarrhoea in 1998 when compared with 1997. All cases of fever or diarrhoea treated in the district hospital in 1998 improved. No case of severe oliguria or anuria was seen by the district hospital. However, a private specialized hospital in Gurgaon town reported that 5 patients with acute renal failure had been seen there. These patients had been treated by local private practitioners for minor illnesses before developing acute renal failure.

There were no apparent links between the cases except that most of the children either lived in the Gurgaon district or had visited Gurgaon town for treatment of a minor illness before developing acute renal failure. It was later found, however, that 15 of 25 (60%) children for whom treatment histories were available had attended the same private clinic in Gurgaon town, which was managed by a qualified paediatrician. Unfortunately, this paediatrician did not have any records of treating these children. Although he admitted that he had treated some children for fever or respiratory illness or watery diarrhoea before they developed anuria, he was surprised that many of them had developed acute renal failure. He also admitted that he prescribed antibiotics, acetaminophen syrup, cough syrup, or oral rehydration salts to these children. All these medicines were given to patients from his dispensary. He also said that he had not changed his treatment practices or any other aspect of his practice recently. He was curious to know why only some of the children he had treated had developed acute renal failure, because he treated a large number of cases (about 100) every day.

Clinical profile of cases

None of the children had had any significant illness in the past. All of them had been treated for minor illnesses (fever, cough, or diarrhoea) by local private practitioners before developing severe oliguria or anuria. Clinical examination after admission to the hospitals in Delhi revealed that most of them were well hydrated. Their vital signs were stable as were most of their haemodynamic functions. There was no significant organomegaly. Their chests were clear. The occasional patient had high blood pressure. There was no evidence of focal neurological lesions.

All children were given peritoneal dialysis as well as supportive treatment. Altogether, 33 (92%) of them died. On average, patients died within 7 days (range 1–24 days) of hospitalization. Thirteen (38%) died within

3 days of hospitalization. Of the 2 patients discharged after improving, one remained in hospital for 10 days and the other for 13. The patients who died were not clinically different from those who survived.

Laboratory investigations

Laboratory investigations revealed that blood urea concentrations (n = 21; median 150 mg/dl, range 79–311 mg/dl) and serum creatinine concentrations (n = 29; median 5.6 mg/dl; range 2.6–10.8 mg/dl) were high. Sodium concentrations were within the normal range, but potassium concentrations were markedly increased in most children. Analysis of blood gases showed that most patients were acidotic. There was a mild to moderate increase in liver enzymes alanine aminotransferase (n=10; 129 mg/dl, range 22–480 mg/dl; and in 11 children median aspartate aminotransferase (n=11; median 130 mg/dl, range 26–416 mg/dl). Serum bilirubin concentrations remained within the normal range in most of the cases; 9 children had median concentrations of 0.9 mg/dl (range 0.3–1.6 mg/dl). In the few children who were able to pass 5–10 ml of urine, the urine showed a specific gravity of 1015-1020, a large number of red blood cells, but no casts. Coagulation profiles were within normal limits. One patient had thrombocytopenia. Chest radiographs were normal in all cases. Kidney biopsy done on 2 children at the Kalawati Saran Children's hospital identified acute tubular necrosis.

Four children who could be tested were found negative for IgM and IgG antibodies against dengue. They also tested negative for antibodies against respiratory viruses (influenza, respiratory syncytial virus, and adenovirus) and Hantaviruses. Only 1 of 4 cases tested had antibodies against cytomegalovirus. Of the 15 patients who could be tested all were negative for antibodies against coxsackie B_{1-6} viruses. All but one (titre 1:32) cases tested negative for antibodies against enterovirus 71.

Stool samples from 16 cases were processed for isolation of enteroviruses. Two of them yielded polioviruses (further typing was not done), one was positive for nonpolio enteroviruses, and two were positive for a mixture of enteroviruses which were not typed further. No virus could be grown from the stool samples of 11 cases or blood samples from 17 cases.

Stool samples from 4 cases were processed for *Salmonella* spp, *Shigella* spp, *Aeromonas* spp, and *Vibrio cholerae O:1* and *O:139*; these pathogens were not identified. However, yeast cells were grown in all of these samples. These samples were also negative for enterohaemorrhagic *Escherichia coli* and rotavirus. Of 12 blood samples cultured for bacterial pathogens, only one was positive for *Klebsiella* spp.

Stool and blood samples from many of the household and community contacts of the children were also processed for viral and bacterial pathogens. Of 27 stool samples from contacts, 6 yielded echoviruses types 4, 6, 9 (2 samples), 11, 12 and 25 (2 samples), while one each was positive for group B coxsackievirus and nonpolio-enteroviruses,

Fig. 1. **Outbreak-associated cases of acute renal failure in two hospitals in Delhi by day of admission, 1998**

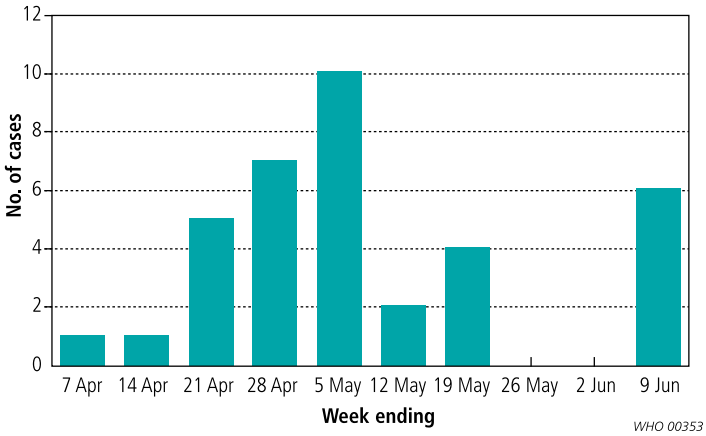

Table 1. **No. (%) of children with acute renal failure caused by contaminated medicine in Gurgaon, India, 1998, by age and sex**

Age (months)	Boys	Girls	Total	Deaths	Case fatality rate (%)
0–5	3 (8.3)	2 (5.6)	5 (13.9)	4	80
6–11	9 (25)	2 (5.6)	11 (30.6)	11	100
12–23	7 (19.4)	3 (8.3)	10 (27.8)	9	90
24–35	3 (8.3)	2 (5.6)	5 (13.9)	4	80
36–72	3 (8.3)	2 (5.6)	5 (13.9)	5	100
Total	**25 (69.4)**	**11 (30.6)**	**36 (100)**	**33**	**92**

Table 2. **No. of children <13 years old with pyrexia of unexplained origin or diarrhoea who attended the outpatient department of the General Hospital, Gurgaon, India, between January 1997 and April 1998**

	Pyrexia of unexplained origin		Diarrhoea	
	1997	1998	1997	1998
January	95	19	105	6
February	96	26	85	17
March	158	53	99	18
April	116	71	168	61
May	168		130	
June	264		170	
July	427		174	
August	223		143	
September	221		146	
October	267		141	
November	172		98	
December	160		82	

which could not be typed. Stool samples from 27 contacts were processed for *Salmonella* spp, *Shigella* spp, *Aeromonas* spp, and *V.cholerae O:1*and *O:139*. One sample each yielded *Shigella sonnei*, *Salmonella typhi*, and yeast cells. The remaining 24 were negative. All 27 stool samples were also negative for enterohaemorrhagic *Escherichia coli* and rotavirus. No virus or bacterial pathogen could be isolated from five blood cultures taken from contacts. These blood samples were also negative for antibodies against enterovirus 71.

An unacceptably high number of coliform organisms were found in drinking-water samples from the household of one case (>180/100ml) and two samples from a nearby village (5/100 ml and 17/100 ml respectively).

Of the six drug samples tested by the Central Drugs Laboratory, Calcutta, one (a brand of cough expectorant manufactured by a company in Gurgaon) was found by gas liquid chromatography to contain 17.5% (v/v) diethylene glycol; this sample also contained 4.25 mg bromhexine Hcl and 27.4 mg of pseudoephedrine Hcl per 5 ml when tested by thin layer chromatographic densitometry. A sample of acetaminophen syrup manufactured by the same company was not contaminated. Four more samples (including paracetomol or cough syrup) manufactured by two other companies were also free from diethylene glycol; one sample of cough syrup, however, contained ethylene glycol. Details are shown in Table 3.

Discussion

At the beginning of the investigation we never imagined that contaminated medicine was causing acute renal failure in children. Virtually all cases of unexplained acute renal failure in this series began with an acute febrile illness with or without watery diarrhoea or mild respiratory symptoms, and quickly ended in the complete shutdown of the patient's kidneys. None of the children were dehydrated or in hypovolaemic shock when admitted to the hospitals in Delhi, and most did not respond to peritoneal dialysis and conventional treatment for renal failure. The paediatric nephrologist at Kalawati Saran Children's Hospital ruled out haemolytic uraemic syndrome or acute tubular necrosis caused by severe dehydration or shock as the possible cause of acute renal failure.

There were no apparent connections between the cases except that almost all of them either lived in the Gurgaon district or in the surrounding areas and a large proportion of them (15/25) had attended a private clinic in Gurgaon town before developing acute renal failure. Field visits to the areas in the Gurgaon district from where the patients came revealed that there was no history of any other case or death associated with anuria or severe oliguria in these areas, and that only a few sporadic cases of fever or diarrhoea had occurred. These observations and data on cases of fever and diarrhoea from the district hospital indicated that there had been no outbreak of fever, diarrhoea, or any other recognizable illness. These observations also indicated that transmission was probably not occurring through person-to-person contact.

However, in light of the gastrointestinal symptoms present in many of the children, the widespread contamination of water, and our knowledge of hygienic practices, agents that could be transmitted by the faecal-oral route were investigated: enteroviruses can cause subclinical infection and acute renal failure. We screened a large number of blood and stool samples from cases as well as from their household and community contacts. The results did not indicate that enteroviruses had played a part in the high number of cases of acute renal failure.

The importance of the finding that a large number of the children had attended a private clinic in Gurgaon town before developing acute renal failure was not immediately clear. The investigators met the paediatrician at the clinic many times without coming to any conclusions. It was obvious, however, that he and many other private practitioners were using antibiotics, such as cephalosporines and aminoglycosides, especially in injectable form, to treat cases of minor illness, including watery diarrhoea. Many of the children who developed acute renal failure had received these antibiotics at this clinic. These medicines are potentially nephrotoxic, especially if used in large doses or in patients with pre-existing renal disease. Patients being treated with these medicines require monitoring of their renal function; this was not done at this clinic. Pathogens such as *S. typhi* rapidly develop resistance if antibiotics are used indiscriminately.

The breakthrough came after an article appeared in *JAMA* describing an upsurge in deaths among children caused by acute renal failure which had occurred in Haiti when acetaminophen syrup was contaminated with diethylene glycol (*4*). This paper also reviewed other cases of diethylene glycol poisoning, including one that occurred in India in 1986. The clinical and laboratory findings observed in these series were similar to those observed in Delhi. The availability of biopsy reports indicated the possibility of toxic renal injury. The paediatrician at whose clinic a large proportion of children had been treated had used liquid medicines (including acetaminophen syrup and cough syrup) manufactured by a company in Gurgaon. Consequently, the National Institute of Communicable Diseases immediately informed the Drug Controller General about the unusual clustering of cases of acute renal failure among children admitted to hospitals in Delhi and the possibility that the contamination of medicine might be responsible. The finding that diethylene glycol was present in a large concentration in one of the samples evaluated by the drug controller led to the conclusion that it was probably the cause of acute renal failure in the children seen in Delhi.

A brand of cough expectorant manufactured by a local pharmaceutical company was found by the

Table 3. **Results of medicines tested for contamination**

Name of company and address	Name of drug tested (batch no.)	Contents	Quantity claimed per 5 ml	Quantity found per 5 ml	Method[a]	Remarks by the laboratory
NR, Gurgaon (Haryana)	Enchest expectorant (2366)	Bromhexine Hcl	4 mg	4.25 mg	TLC Densitometry	• The sample is considered to be not of standard quality for the presence of diethylene glycol
		Pseudoephedrine Hcl	30 mg	27.4 mg	TLC Densitometry	
		Diethylene glycol	nil	17.5% (v/v)	GLC	
	Nobemol suspension (2371)	Paracetamol	125 mg	104 mg	TLC Densitometry	• The sample does not confirm claim with respect to the content of paracetamol (low) • The sample is included in United States Pharmacopoeia (USP) and should be labelled accordingly • Addition of colour in paracetamol suspension is not official in USP • Additional test for glycols: negative for ethylene glycol and diethylene glycol test (GLC)
SC, Faridabad (Haryana)	Decoryl suspension (413)	1-Phenylephrine Hcl	1.5 mg	1.387 mg	Colorimetric	• The sample is considered to be not of standard quality due to the presence of ethylene glycol
		Acetaminophen	125 mg	121.11 mg	Colorimetric	
		Chlorpheniramine maleate	2 mg	1.929 mg	Spectrophotometric after separation	
		Ethylene glycol	nil	0.5067% (v/v)	GLC	
	Prestigin suspension (492)	Ibuprofen	100 mg	90.60 mg	Titrametric after separation	• The sample conforms to claim with respect to above tests • The sample does not give positive tests for ethylene glycol and diethylene glycol (GLC method)
		Paracetamol	125 mg	134.03 mg	Colorimetric	
EAIR, Bahadurgarh (Haryana)	Recovil suspension (D-88)	Promethazine Hcl	125 mg	2.354 mg	Colorimetric after separation	• The sample conforms to claim with respect to above tests • The sample does not give positive tests for ethylene glycol and diethylene glycol (GLC method)
		Paracetamol	125 mg	121.8 mg	Colorimetric	
	Q-Flor suspension (B-228)	Ciprofloxacin	125 mg	119.39 mg	Spectrophotometric	• The sample conforms to claim with respect to above tests • The sample does not give positive tests for ethylene glycol and diethylene glycol (GLC method)

[a] TLC, thin layer chromatographic densitometry; GLC, gas-liquid chromatography.

Central Drugs Laboratory, Calcutta, to contain 17.5% (v/v) diethylene glycol. A sample of acetaminophen syrup manufactured by the same company was not contaminated. Both of these medicines had been used by the paediatrician in Gurgaon to treat children who later developed acute renal failure. The absence of diethylene glycol in the acetaminophen syrup probably explains why only a small proportion of children treated by the paediatrician developed renal failure. Almost all doctors prescribe liquid acetaminophen to children with fever. If the acetaminophen syrup had been contaminated, many more children over a larger geographical area would have developed renal failure, as was the case in Haiti and Bangladesh (*4, 5*).

Some patients who were not treated by this paediatrician but were treated by other private medical practitioners also developed renal failure. Since all of the children were given unlabelled liquid medicines, it is not possible to say whether these children received the same cough syrup, whether some other medicines

were also contaminated, or whether medicines manufactured by other companies were also contaminated. Providing medicines to patients without labels is dangerous and needs immediate attention. The absence of labels affected our epidemiological investigations. We could not determine whether children with renal failure had received medicine that was different from those who did not develop renal failure. Such data would have helped us discover the cause much earlier and saved lives.

Without further investigations, many questions could not be answered. It would be helpful to discover where the diethylene glycol came from, at what point in the process contamination occurred, and whether the contamination was accidental. Additionally, we need to ask how a contaminated medicine was released onto the market. The government of Haryana has convened a fact-finding committee to investigate. Nevertheless, this contamination, as well as others previously reported, indicate that there are major problems in enforcing pharmaceutical legislation in developing countries.

The district and state drug controller had tested many samples using thin layer chromatography before a sample of medicine tested positive for diethylene glycol at the Central Drugs Laboratory. None of the earlier samples was found to be contaminated. These samples included the same brand and same batch of cough expectorant later found to be highly contaminated when tested using gas-liquid chromatography. This indicates that thin layer chromatography alone may not identify contamination with diethylene glycol. On the other hand, gas-liquid chromatography or other appropriate methods are not available in all the laboratories that may be asked to test medicines. Appropriate tests must be available in laboratories that test medicines for contaminants.

The failure to detect the contamination using thin layer chromatography had an important bearing on these cases. Once contamination was suspected and the samples were sent for testing, the number of cases suddenly declined (Fig.1). After the samples were declared not to be contaminated, 6 more cases occurred. Further cases were only stopped because scientists continued to suspect contamination and insisted that the suspect medicines should not be used unless found to be uncontaminated using gas-liquid chromatography.

The epidemiological, clinical, and laboratory investigations strongly implicated diethylene glycol as the cause of the initially unexplained cases of acute renal failure among children, which claimed 33 lives. Contamination of or substitution in medicines of diethylene glycol has occurred in many countries, including Argentina, Bangladesh, Nigeria, Haiti, and India, and it has resulted in the loss of over 500 lives (*6*). Problems related to the enforcement of pharmaceutical legislation must be addressed to prevent the reoccurrence of such tragedies. ■

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Résumé

Intoxication par le diéthylène glycol à Gurgaon (Inde) en 1998

Objectif Découvrir la cause d'une insuffisance rénale aiguë chez 36 enfants âgés de 2 mois à 6 ans ayant été admis dans deux hôpitaux de Delhi entre le 1er avril et le 9 juin 1998.

Méthodes On a rassemblé des données en examinant les dossiers des hôpitaux et en interrogeant les parents et les médecins des enfants atteints ainsi que les responsables sanitaires du district. Des visites domiciliaires et des enquêtes en communauté ont permis d'obtenir des informations complémentaires ; on a prélevé des échantillons de sang et de selles sur d'autres enfants malades, sur des membres en bonne santé de la famille et sur des contacts communautaires. On a également fait des recherches de colibacilles dans des échantillons d'eau de boisson et d'eau provenant d'un puits tubé.

Résultats La plupart des enfants (26/36) venaient du district de Gurgaon dans l'Etat d'Haryana ou avaient séjourné à Gurgaon pour le traitement d'une affection mineure. L'insuffisance rénale aiguë est apparue après un épisode fébrile avec ou sans diarrhée aqueuse ou symptômes respiratoires bénins, traité avec des médicaments de nature inconnue par un médecin du secteur privé. A l'admission, les enfants n'étaient pas déshydratés. L'azote uréique sanguin médian était de 150 mg/100 ml (intervalle : 79–311 mg/100 ml) et la créatinine sérique médiane était de 5,6 mg/100 ml (intervalle : 2,6–10,8 mg/100 ml). Une biopsie rénale a montré une nécrose tubulaire aiguë. On sait que 33 enfants sont décédés malgré une dialyse péritonéale et un traitement de soutien.

Conclusion Un expectorant contre la toux fabriqué par un laboratoire de Gurgaon a été trouvé contaminé par du diéthylène glycol (17,5 % v/v), mais aucune contamination n'a été décelée dans un échantillon d'acétaminophène du même fabricant lors d'une analyse par chromatographie gaz-liquide. Une intoxication par le diéthylène glycol semble donc avoir été à l'origine de l'insuffisance rénale aiguë chez ces enfants.

Resumen

Intoxicación por dietilenglicol en Gurgaon (India) en 1998

Objetivo Descubrir la causa de la insuficiencia renal aguda padecida por 36 niños de 2 meses a 6 años de edad ingresados en dos hospitales de Delhi entre el 1 de abril y el 9 de junio de 1998.

Métodos Los datos empleados proceden de historias clínicas y de la información aportada por los padres y los médicos de los pacientes y por funcionarios de salud de distrito. Se reunió también información a partir de visitas domiciliarias y encuestas comunitarias. Se obtuvieron muestras de sangre y de heces de otros niños enfermos, de familiares sanos y de contactos de la comunidad, y se analizó la presencia de microorganismos coliformes en muestras de agua de bebida y de agua de un pozo entubado.

Resultados La mayoría de los niños (26/36) procedían del distrito de Gurgaon, en Haryana, o habían visitado la localidad de Gurgaon para recibir tratamiento contra una enfermedad de poca gravedad. La insuficiencia renal aguda se produjo tras un episodio febril agudo, en algunos casos acompañado de diarrea acuosa o de síntomas respiratorios leves, contra el cual médicos privados habían recetado medicamentos de naturaleza desconocida. Al ingresar en el hospital los niños no estaban deshidratados. La mediana de la concentración de nitrógeno ureico en sangre fue de 150 mg% (intervalo: 79-311 mg%), y la de la concentración sérica de creatinina, de 5,6 mg% (intervalo: 2,6-10,8 mg%). La biopsia renal reveló una necrosis tubular aguda. Se sabe que 33 niños fallecieron pese a ser sometidos a diálisis peritoneal y terapia complementaria.

Conclusión Se descubrió que un expectorante fabricado por una compañía de Gurgaon estaba contaminado por dietilenglicol (17,5% v/v); sin embargo, los resultados de un análisis por cromatografía gas-líquido de una muestra de paracetamol fabricada por la misma compañía fueron negativos. Así pues, la causa de la insuficiencia renal aguda sufrida por esos niños parece haber sido una intoxicación por dietilenglicol.

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