eficial in patients with diabetes mellitus. Further research is clearly needed to understand how and why, as reported by Tsalamandris et al, some patients with diabetes lose renal function in the absence of albuminuria.

Holly Kramer, MD, MPH
Department of Epidemiology and Preventive Medicine
Loyola University Medical Center
Maywood, Ill

Chi-yuan Hsu, MD, MSc
Division of Nephrology
University of California at San Francisco

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RESEARCH LETTER

Methyl Isocyanate Exposure and Growth Patterns of Adolescents in Bhopal

To the Editor: More than 200 000 people were exposed to methyl isocyanate (MIC) and other gases following the Union Carbide (UC) Pesticide Plant incident at Bhopal, India, on December 3, 1984; in addition to thousands of deaths from acute exposure, this incident has resulted in chronic health problems.[1-3] We measured the effects of exposure to fumes from the incident on the physical growth pattern of adolescents.

Methods. Between May 10 and June 30, 2001, we made anthropometric measurements in exposed adolescents as well as in age- and sex-matched unexposed individuals.

The exposed individuals lived within 1 km northeast of the UC plant at the time of the incident; this area recorded a death rate of more than 3% (150 times the normal rate) within a week of the incident.[4] The unexposed individuals lived in localities 15 km southwest or 4 km northwest of the factory; these areas were not affected because of the distance and wind direction. Households for survey were chosen randomly; all identified households except 2 provided written informed consent to participate in the study.

The survey team led by a social worker was from a different town and had no prior knowledge of the health of the adolescents. The team recorded body weight, height, sitting height, mid-arm circumference, head circumference, and triceps skinfold of the adolescents, as well as the height, weight, and socioeconomic status of their parents. Ages were based on birth certificates if available, and otherwise on a "people's calendar" relating to important local events/festivals, horoscopes, parental diaries, and ages of other siblings.

The data were analyzed separately for boys and girls by analysis of covariance with 4 groups (unexposed, postnatal exposure, in utero exposure, and preconception exposure [ie, born after the incident to exposed parents]) and 6 potential covariates: age, mother's height and weight, father's height and weight, and socioeconomic status (per capita monthly income above or below Rs 750 [approximately US $15]). For each outcome variable for each sex, only the covariates that were statistically significant at $P<.05$ were retained in the final model. All analyses were performed using SAS version 8.2 (SAS Institute Inc, Cary, NC) using multiple regression, with the 3 types of exposure forced into the model. The number of families with 2 boys (n=6) or 2 girls (n=14) was too small to permit a rigorous analysis of sibling correlation. Instead, analyses were repeated with only 1 child from each family.

Results. The study included 104 families with 68 girls and 73 boys, with 71 of the adolescents exposed to the gases (mean age, 16.9 [SD, 1.3] years) and 70 unexposed (mean age, 16.7 [SD, 1.4] years). The mean (SD) body weights and heights of exposed and unexposed mothers were similar (48.2 [10.1] vs 49.1 [9.0] kg; 149 [5] vs 151 [5] cm), as were those of exposed and unexposed fathers (54.6 [12.3] vs 53.4 [8.9] kg; 163 [6] vs 162 [6] cm). TABLE 1 presents the outcome variables

Table 1. Outcome Variables by Sex, Age, and Exposure to Gases From the Union Carbide Plant Disaster in Bhopal, 1984*

	Girls				Boys			
	Born Before Disaster		Conceived After Disaster		Born Before Disaster		Conceived After Disaster	
Variable	Exposed (n = 20)	Unexposed (n = 16)	Exposed (n = 11)	Unexposed (n = 14)	Exposed (n = 28)	Unexposed (n = 23)	Exposed (n = 6)	Unexposed (n = 8)
Weight, kg	42.1 (6.2)	42.3 (4.3)	38.4 (5.6)	38.2 (5.0)	44.1 (7.7)	46.4 (4.9)	32.6 (2.1)	43.5 (6.6)
Height, cm	148.6 (3.7)	148.5 (5.3)	148.8 (4.7)	148.6 (6.1)	161.2 (9.3)	164.6 (5.0)	145.7 (3.2)	158.8 (7.7)
Sitting height, cm	75.6 (4.3)	76.9 (3.1)	75.8 (4.0)	77.5 (2.9)	80.0 (5.0)	82.7 (2.8)	71.0 (2.5)	78.5 (4.5)
Mid-arm circumference, cm	21.7 (2.4)	21.6 (1.5)	19.8 (1.8)	19.7 (1.2)	20.7 (2.2)	21.9 (1.1)	18.0 (1.1)	20.3 (1.6)
Head circumference, cm	52.1 (1.3)	52.2 (0.9)	51.8 (1.0)	52.3 (1.1)	53.0 (1.7)	53.3 (1.2)	51.3 (0.8)	52.8 (1.2)
Triceps skinfold, mm	11.3 (3.1)	10.4 (3.0)	9.1 (3.3)	8.2 (1.6)	6.5 (2.4)	5.4 (1.4)	5.4 (0.8)	5.7 (1.4)
Body mass index†	19.1 (3.0)	19.2 (1.4)	17.3 (2.3)	17.3 (1.7)	16.8 (1.7)	17.1 (1.6)	15.3 (0.4)	17.2 (1.1)

*All values are mean (SD).
†Calculated as weight in kilograms divided by the square of height in meters.

Table 2. Effect in Boys of Exposure to Gases From the Union Carbide Plant Disaster in Bhopal, 1984

Variable	Postnatal Exposure (n = 28 Born Before Disaster)		In Utero Exposure (n = 3 Exposed as Fetus)		Preconception Exposure (n = 6 Conceived After Disaster)	
	Effect (95% CI)*	*P* Value†	Effect (95% CI)*	*P* Value†	Effect (95% CI)*	*P* Value†
Weight, kg	–2.8 (–5.7 to 0.1)	.06	–10.0 (–16.0 to –3.0)	.003	–7.9 (–13.0 to –2.0)	.007
Height, cm	–3.9 (–7.4 to –0.4)	.03	–13.5 (–21.0 to –6.0)	.001	–8.4 (–15.0 to –1.0)	.02
Mid-arm circumference, cm	–0.9 (–1.7 to –0.1)	.03	–2.7 (–4.6 to –0.8)	.005	–2.0 (–3.5 to –0.5)	.01
Head circumference, cm	–0.09 (–0.8 to 0.6)	.77	–3.2 (–4.8 to –1.5)	<.001	–1.6 (–2.8 to –0.4)	.009
Triceps skinfold, mm	1.0 (0.1 to 1.9)	.03	1.9 (–0.3 to 4.0)	.09	0.3 (–1.3 to 1.9)	.73
Body mass index‡	–0.3 (–0.9 to 0.4)	.46	–1.3 (–2.9 to 0.3)	.11	–1.4 (–2.6 to –0.2)	.03

Abbreviation: CI, confidence interval.
*Effects reported are of each type of exposure on anthropomorphic measures at follow-up, relative to the 36 unexposed boys. Values reported are regression coefficients, equal to the differences between exposed and unexposed boys in Table 1, after adjustment for age, mother's weight, mother's height, father's height, and socioeconomic status. Thus, the effect of postnatal exposure on height is –3.9 cm,.meaning that the boys exposed to the gases were 3.9 cm shorter than unexposed boys of the same age and with the same parental weight and height; the difference in Table 1 is –3.4 cm before adjustment. The effect of preconception exposure on weight is –7.9 kg after adjusting the –10.9 kg difference in Table 1 for covariates, meaning that the boys conceived by exposed parents weighed 7.9 kg less than unexposed boys of the same age and parental weight and height.
†For comparison of effects with zero.
‡Calculated as weight in kilograms divided by the square of height in meters.

for the various combinations of exposure and sex. Data for the few individuals who were exposed in utero (exposed: 3 boys, 3 girls; unexposed: 5 boys, 4 girls) were included in the statistical analysis but are not shown in Table 1. There was no significant effect of any type of exposure, including in utero exposure, in girls. However, exposure was associated with significant decreases in most anthropometric measures in boys (TABLE 2). The exposed boys had lower levels of several anthropometric variables, although their triceps skinfold measurements were greater. The exposure effect was most pronounced in boys exposed in utero and least severe in boys born before the incident. The analysis of covariance showed no significant effect of exposure on the growth pattern of girls. Repeating the analyses with only 1 child from each family yielded essentially identical results.

Comment. We found selective growth retardation in boys, but not in girls, who were either exposed as toddlers to gases from the Bhopal pesticide plant or born to exposed parents. The fact that exposed and unexposed girls were virtually identical in all measures suggests that the exposed and unexposed groups were well-matched and that the association observed in boys is truly a result of exposure and not of other unobserved differences in the demographics. The main chemical that escaped from the plant was MIC, which is readily degraded on contact with water and in the body.[1-3] One of the degradation products of MIC is trimethylamine, which has been reported to produce selective growth retardation of male progeny of mice, associated with a decrease in serum testosterone.[5] It is possible that similar hormonal effects were produced by MIC, its metabolites, or other substances.

Nishant Ranjan, BA
Satinath Sarangi, MTech
V. T. Padmanabhan, MPhil
Sanbhavna Clinic
Bhopal, India

Steve Holleran, BA
Rajasekhar Ramakrishnan, ScD
Department of Pediatrics
Columbia College of Physicians and Surgeons
New York, NY

Daya R. Varma, MD, PhD
Department of Pharmacology
McGill University
Montreal, Quebec

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