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TO THE EDITOR: Air pollution does have an adverse effect on the lungs of children, and interventions to improve air quality can decrease lung diseases. In Ahmadabad, Gujarat, India, public transportation consisted of diesel-powered buses and three-wheeled automobiles powered by kerosene-adulterated gasoline. Hospital admissions for asthma and bronchiolitis steadily increased over a 5-year period until the government decided to order the conversion of all buses and automobiles to run only on compressed natural gas. A year later, admissions for asthma and bronchiolitis (diagnosed clinically) had declined, as had the number of new cases of asthma at the asthma clinic.

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THE AUTHOR REPLIES: In response to Bates and Hogg, it is very likely that the amount of carbon in airway macrophages of healthy persons reflects the exposure of other airway cells to inhaled particles. Persistent subepithelial fibrosis and remodeling caused by the direct effect of particles on bronchiolar cells would explain why, in our study, bronchodilator therapy had no effect on the inverse association between the carbon content of airway macrophages and lung function in healthy children.

Bruce et al. rightly point out that on a global scale, particulate matter from the burning of biomass fuel is a major environmental health threat to children. Recently, my colleagues and I reported that particles from biomass smoke rapidly deplete antioxidants in the epithelial lining fluid of the lung.[1] The analysis of induced sputum, which contains cells and antioxidants from the lower airways, may therefore be a useful addition to studies of the mechanism of the effects on health of biomass smoke in the developing world.

Citywide initiatives similar to the one reported by Gohil have been invaluable for identifying particles as the major toxic component of air pollution.[2] Measuring the effect of air-pollution initiatives on human health requires ongoing collaboration among local council officials, nongovernmental organizations, and air-pollution scientists.

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N-Acetylcysteine and Contrast-Induced Nephropathy

TO THE EDITOR: The primary end point of the study by Marenzi et al. (June 29 issue)[1] was the occurrence of contrast-medium–induced nephropathy, defined as an increase in the serum creatinine concentration of 25% or more from the baseline value within the 72-hour period after primary angioplasty. The reported incidence of contrast-medium–induced nephropathy varies widely among studies, since increases in the level of serum creatinine and the interval after the administration of contrast medium are not uniform among studies. In the Rapid Protocol for the Prevention of Contrast-Induced Renal Dysfunction (RAPPID) trial,[2] contrast-medium–induced nephropathy was defined as a 25% increase in the serum creatinine level either 2 or 4 days after the administration of contrast medium. Briguori et al.[3] and Tepel et al.[4] define contrast-medium–induced nephropathy as an increase in serum creatinine of at least 0.5 mg per deciliter 48 hours after contrast administration. In their recent review article, Barrett and Parfrey[5] state that serum creatinine levels peak 3 days after the administration of contrast medium and that appreciable nephrop-

athy probably will not develop unless the serum creatinine level increases by more than 0.5 mg per deciliter within 24 hours.

Thus, given its clinical relevance, a consensus regarding the definition of contrast-medium–induced nephropathy is urgently needed. Meanwhile, we should take care before comparing the incidence of this complication among trials.

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TO THE EDITOR: Marenzi et al. report that *N*-acetylcysteine reduces the risk of contrast-medium–induced nephropathy after primary angioplasty for acute myocardial infarction with ST-segment elevation. However, these results may not be generally applicable. The in-hospital mortality rate in the control group (11%) was much higher than the rate of 4 to 5% typically reported in recent randomized studies and large registries.[1,2] The authors further report that 5% of patients in the control group required renal-replacement therapy; this very frequent use of dialysis was possibly explained by the authors' liberal threshold for this method of treatment.[3]

We compared the findings of Marenzi and colleagues with our experience in a large teaching hospital. Among 1174 consecutive patients who underwent primary angioplasty, only 3 (0.3%) required dialysis. In the study by Marenzi et al., the mean volume of contrast medium ranged from 253 to 274 ml. At our center, the mean (±SD) volume was 156±70 ml. We think it is likely that in a more typical population of patients with myocardial infarction and ST-segment elevation, no difference in clinical outcome would have been observed, particularly had contrast medium been used more judiciously.

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TO THE EDITOR: Marenzi and colleagues report a reduction in the incidence of contrast-medium–induced nephropathy and in-hospital mortality associated with primary angioplasty among patients receiving *N*-acetylcysteine. Nevertheless, there was no difference in the incidence of acute renal failure requiring renal-replacement therapy, a relevant clinical predictor of mortality related to renal impairment induced by contrast medium.[1,2] This finding suggests that the difference in in-hospital mortality might have been related more to depressed left ventricular function than to renal impairment. Thus, it would be of interest to know the initial hemodynamic status and renal function of the patients in whom cardiogenic shock and heart failure leading to death occurred, especially because the control group had a surprisingly high mortality rate.

In addition, the combined end point calls for careful review. The definition used may not be correct, since the requirement for mechanical ventilation depended on cardiogenic shock, the main cause of death in the study.

Although the authors reported a dose-dependent protective effect of *N*-acetylcysteine, the two *N*-acetylcysteine groups had similar rates of contrast-medium–induced nephropathy (15% in the standard-dose group and 8% in the high-dose group, P=0.13), renal-replacement therapy, and death.

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TO THE EDITOR: The article by Tepel et al.[1] on the use of *N*-acetylcysteine to prevent contrast-agent–induced reductions in renal function provoked a flurry of studies — unfortunately with widely differing results. Research does not obey the democratic rule of the majority, so it does not help to count the number of patients, as a great number of meta-analyses have done. The original study and most of the follow-up studies were conducted on the basis of measurements of serum creatinine. Marenzi et al. provide information on the estimated creatinine clearance in addition to the serum creatinine concentration after angioplasty in patients with acute myocardial infarction. However, a study involving volunteers (admittedly not a study involving patients with acute renal failure) provided indirect evidence that *N*-acetylcysteine affects tubular creatinine transport.[2] As a result, the serum concentration of creatinine was decreased, but not that of cystatin C, a marker of the glomerular filtration rate that is not affected by tubular transport or by other confounders that render the measurement of creatinine somewhat problematic.

It would be helpful if Marenzi and colleagues could show that in their study the concentrations of cystatin C, as an independent marker of the glomerular filtration rate, moved in parallel with those of serum creatinine.

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THE AUTHORS REPLY: Regarding the comments of Ritz, the means to measure cystatin C were not available in our institution at the time of our study, and the results of the study by Hoffmann et al. had not yet been published when we designed our study. Although these may be limitations, it is possible that *N*-acetylcysteine has a protective effect when oxidative stress induced by ischemia and reperfusion plays a role in pathogenesis but has little or no effect when oxidative stress is absent, as is the case in healthy subjects. Moreover, beyond a direct renal effect, the cardioprotective properties of *N*-acetylcysteine may help prevent contrast-medium–induced nephropathy, resulting in improved left ventricular function and renal hemodynamics.

The mortality rate in our control group was higher than that in other recent randomized trials. However, the numerous exclusion criteria used in such trials, which often do not enroll high-risk patients, may explain their invariably lower mortality rate as compared with the rates in primary angioplasty registries. Indeed, a mortality rate between 9.3 and 10.8% was reported in some recent studies, reflecting, as in our study, "real-world" clinical practice.[1-3]

We agree with Aguiar-Souto and colleagues that because of the variety of definitions of contrast-medium–induced nephropathy (absolute or relative increases in creatinine 24, 48, or rarely 72, 96, or 120 hours after exposure to contrast medium), a consensus is needed. Indeed, because creatinine peaks between the fourth and fifth day, contrast-medium–induced nephropathy may be missed in many patients if one relies only on measurements made during the first 48 hours.[4]

We used hemodialysis and hemofiltration as renal-replacement therapies. However, of the nine patients who received renal-replacement therapy (2.5%), only one (0.3%) underwent hemodialysis, whereas the remaining eight (2.3%) underwent hemofiltration, which was mainly started earlier than the "standard" indication for hemodialysis because of overt pulmonary congestion. Thus, renal-replacement therapy was not directly correlated with the occurrence of acute renal failure.

The amount of contrast medium used in our study was similar to that reported by others and reflects our practice of primary percutaneous coronary intervention, including left ventriculography performed to assess left ventricular function and to exclude ventricular septal defect and mitral-valve regurgitation; optimal stent deployment, which often requires an increased number of angiographic projections in order to reduce the risk of thrombosis; and the use of thrombus aspiration or distal protection systems in case of a

large thrombus burden. Indeed, a recent study comparing clinical and procedural characteristics among hospitals, mostly regarding elective percutaneous coronary intervention, invariably reported a contrast volume of more than 200 ml.[5]

Finally, the difference in the primary end point and the other clinical end points between the two *N*-acetylcysteine groups was significant when analyzed by the Mantel–Haenszel chi-square test for trend, suggesting a dose-dependent protective effect of *N*-acetylcysteine.

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Iodine Nutrition — More Is Better

TO THE EDITOR: The editorial by Utiger (June 29 issue)[1] summarizes the effects of iodine deficiency. However, his recommendation of an iodine intake of 300 to 400 μg per day far exceeds the following recommendations of the Institute of Medicine: 150 μg per day for nonpregnant adults, 220 μg per day for pregnant women, and 290 μg per day during lactation.[2] Teng et al.[3] found that an iodine intake of approximately 320 to 840 μg per day resulted in an increased incidence of subclinical hypothyroidism and thyroid autoimmunity. These risks may be clinically important — children of women with subclinical gestational hypothyroidism may have neurocognitive delays.[4] Utiger suggests that iodine intake in the United States is marginal on the basis of the prevalence of spot urinary iodine values under 50 μg per liter among pregnant women.[5] However, iodine deficiency may not be diagnosed from analysis of spot urine samples in individuals because of day-to-day variability. Median spot urinary iodine values accurately reflect the iodine nutrition of populations, and the median value of 168 μg per liter for the United States[5] is consistent with iodine sufficiency according to World Health Organization (WHO) criteria. We believe that the evidence supports the current guidelines for dietary iodine intake and that overall iodine intake in the United States remains sufficient.

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TO THE EDITOR: We fully agree with the title of Utiger's editorial, "Iodine Nutrition — More Is Better," but wish to comment on how much more is better during pregnancy and lactation.

In January 2005, the WHO held a technical