Metabolic and ventilatory depression in rat

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TO THE EDITOR: The purpose of this letter is to further discuss the possible meaning of some of the results of the study of Stein et al. (14) in the light of previous publications on the effects of H2S and hypoxia exposure on metabolism and breathing control.

Unlike mice, adult rats have already been shown to be insensitive to H2S-induced hypometabolism, at least during 30–60 min of exposure to inhaled H2S (60–80 ppm) (6). The lack of metabolic effect of H2S in a small mammal is not unexpected: we found that the effect of inhalation, or lack thereof, of 60 ppm H2S on metabolism was mirrored by the metabolic response to hypoxia (6). Hypoxia-induced hypometabolism is size dependent (4, 11) but also species related, because, for a given size, mammals appear to reduce their metabolism in hypoxia to a different degree (3). The hypothalamic structures controlling the sympathetic outflow to the brown fat tissue, regulating uncoupling protein activity, contributes to the metabolic depression induced by hypoxia (8). This metabolic reduction depends therefore on the contribution of brown fat tissue to the total metabolic rate and the ability of a given species to reduce this neural activity (10). In other words, the blunted or absent metabolic depression during exposure to H2S in large rats (6) may well depend on aptitude to decrease uncoupling-related O2 consumption (12), regardless of the ability of a given species to oxidize H2S.

An additive metabolic depression produced by H2S (60 ppm) and hypoxia (10% FiO2) has already been reported in mice (6). This effect was also found in rats by Stein et al. (14) based on a decrease in temperature, used as a substitute for metabolism, but only after 5 h of exposure. Whether this delayed reduction in temperature is attributable to a reduction in nonshivering thermogenesis, as in the mice, remains to be established. Indeed, the much lower SaO2 found during combined H2S and hypoxia than with hypoxia alone suggests that an additional hypoxemia resulted from H2S-induced pulmonary toxicity (2, 9). This could have in turn reduced the metabolic rate, masking the severity of this additional hypoxemia. Finally, the inhibitory effects on motor, and thus metabolic, activity of painful irritation produced by H2S toxicity on the lungs, eyes, and skin remain to be investigated. Similarly, breathing frequency (f) was found to decrease more when H2S was combined with hypoxia. Several hours of exposure to H2S-induced airway inflammation could have certainly altered vagal feedback, making the putative mechanisms of this response difficult to ascertain.

Finally it has already been argued that the high metabolic rate per kilogram of weight of small mammals, like mice, is mostly devoted to heat—and not ATP (12)—production and allows O2 consumption to drop without altering vital cellular metabolism (10). Humans, similar to other large mammals (3), are unlikely to do so. H2S administration should be reconsidered in view of the lack of hypometabolic effect in a large mammal (7) and of H2S established toxicity.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS
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