



# Literature Reviews

## Hydrogen sulfide attenuates myocardial ischemia-reperfusion injury by preservation of mitochondrial function.

Elrod JW, Calvert JW, Morrison J, et al.  
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**Abstract:** Hydrogen sulfide (H<sub>2</sub>S) has been best known as the toxic and noxious gas emitted from rotten eggs. It is increasingly appreciated to have interesting pharmacological activity and is suspected to normally participate in physiologic processes. In experiments with mice, researchers from Albert Einstein show the gas to be cardioprotective against ischemia.

Mechanically ventilated, anesthetized mice were subjected to 30 min of LAD artery occlusion. Treated mice received 10-500 µg/kg of H<sub>2</sub>S into the LV lumen at time of reperfusion. Infarction of area at risk was reduced by 72% at the optimal dose (50 µg/kg). Hemodynamic function was preserved and there was less evidence of inflammation (decreased numbers of neutrophils in the ischemic myocardium, decreased levels of the proinflammatory cytokine IL-2B, and a substantial decline in leukocyte-endothelial cell inter-

actions). Mitochondria appeared disrupted in the infarcted tissue by histological and biochemical assays. Even though (or perhaps because) H<sub>2</sub>S is a cyanide-like inhibitor of mitochondrial utilization of oxygen, H<sub>2</sub>S protected the mitochondria. In doses used for myoprotection, H<sub>2</sub>S did not impact blood pressure or heart rate in healthy mice instrumented with radiotelemetric monitors, so the beneficial effect of H<sub>2</sub>S is not mediated by hemodynamic alterations. As were the hearts in vivo, isolated myocytes were protected by H<sub>2</sub>S from hypoxia in vitro.

Transgenic mice were constructed to have cardiac restricted overexpression of cystathionine gamma-lyase, one of the two enzymes that can convert sulfur-containing amino acids into H<sub>2</sub>S. The transgenic animals produced approximately twice as much H<sub>2</sub>S in the myocardium as did wild type mice. When subjected to 45 minutes of LAD occlusion followed by 72 hours of reperfusion, the transgenic mice had a 47% reduction of infarction of area at risk.

**Comments:** H<sub>2</sub>S has parallel features with the better-known nitric oxide, subject of a 1998 Nobel. Both are amino-acid-derived gases that are toxic and irritating in more-than-trace concentrations. Both react with hemoproteins, are normally produced by human tissues, and are vasodilators. Both provide substantial protection against myocardial ischemia/reperfusion injuries, at least, so far, in mice (Am J Physiol 2006; 291:H379).

H<sub>2</sub>S has another feature of interest to cardiovascular anesthesiologists. At 80 ppm, the inhaled gas induces a state of reversibly suspended animation in mice (Science 2005; 308:518). Body temperature falls to nearly ambient, and metabolic rate is accordingly reduced. Mice do not ordinarily hibernate, so this pharmacological property of H<sub>2</sub>S is exciting. However, no large mammals (including the proverbial bear) ordinarily undergo hypothermic hibernation, and no large mammals have yet been reported to hibernate in response to H<sub>2</sub>S. So, the dramatic H<sub>2</sub>S-induced hibernation may apply to mice but not to men. It is to be hoped that the myoprotection effect will be a general one.