
5. Stein PD, Henry JW. Clinical characteristics of patients with acute pulmonary embolism stratified according to their presenting syndromes. Chest. 1997;112:974-979.

In reply:

In response to the rebuttal by Kline et al, we agree that a case report provides limited insight and, as previously stated, does not suggest “a failure of a validated decision rules such as the PERC [pulmonary embolism rule-out criteria].” In our discussion, we questioned the relationship between false-negative PERC status, clot burden, and outcomes. Kline et al assume that the complaint of pleuritic chest pain (a finding more common in false-negative PERC patients per this study) is likely to represent a pulmonary infarction, which is more often associated with small distal clots. Instead of the actual variable of clot burden, Kline et al assume that the complaint of pleuritic chest pain (a finding more common in false-negative PERC patients per this study) is likely to represent a pulmonary infarction, which is more often associated with small distal clots.

This assumption is drawn from an article by Stein and Henry, in which patients with pleuritic chest pain (which the labels the “pulmonary infarction” syndrome) were more likely to manifest higher PaO₂ and trended toward lower pulmonary artery pressure than the “isolated dyspnea” group. Care must be used about terminology because Stein and Henry used “pulmonary infarction syndrome” to describe patients with either pleuritic chest or hemoptysis. Overall, it is unclear that the pleuritic chest pain patients in the study by Pollack et al are truly similar to the “pulmonary infarction” group analyzed by Stein and Henry, particularly because the latter also included patients with hemoptysis. Outcomes are not addressed here because our patient case caused us to consider the ramifications of not identifying emboli-positive patients by the PERC who are therefore unlikely to receive anticoagulation and are consequently sent home.

We look forward to these questions being answered in future prospective studies.

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http://dx.doi.org/10.1016/j.annemergmed.2012.07.115

Funding and support: By Annals policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist.


Utility of Sodium Thiosulfate in Acute Cyanide Toxicity

To the Editor:

In the June 2012 issue of Annals, Bebarta et al conducted an elegant animal study examining the efficacy of sodium thiosulfate in the treatment of cyanide toxicity versus hydroxocobalamin, or a combination of the 2 drugs; we commend the authors on their work. However, the study left us contemplating the clinical effects and outcomes on subjects excluded from the data analysis.

Given the complexity and toxicity of cyanide, we understand the safety and ethical issues that must be taken into consideration (laboratory personnel, animal subjects) when designing such a study. Nonetheless, it is important to appreciate the definitions used by the researchers in order to assimilate a complete clinical picture. In this study, each arm defined death as a mean arterial pressure of less than 20 mm Hg for 5 minutes. Although all subjects randomized to the sodium thiosulfate–only group died before completion of the study, it is unclear whether the animals succumbed to the toxin, experienced an adverse effect of the antidote, or met the objective definition of death, raising the question of whether the animals would have shown improvement if only allotted more time for enzyme reactivation. In addition, the variability of enzyme activity between species and chronologic age could also play a role in the efficacy of the antidote.

We hope that further studies will elucidate the effectiveness of sodium thiosulfate in the human population.

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Rhodanese is found in swine at levels similar to that in humans and is also found in the liver in greater levels than other organs, as in humans. 

Age, comorbidities, and individual susceptibility affect rhodanese levels in swine as they do in humans. We agree that human clinical trials are important and better delineate the effectiveness of the chemical toxin antidotes; however, these trials are difficult to conduct because of trial and drug costs, exposure rarity, outcome severity, and range in exposure dose. The “animal rule” is accepted by the Food and Drug Administration as evidence to support countermeasure effectiveness with these uncommon exposures.

Finally, given the overwhelming findings in our study, it would difficult to recommend sodium thiosulfate alone.

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Funding and support: By Annals policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist. The US Air Force Office of the Surgeon General funded this study.

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