parenteral routes, but did not find that they had been associated with hypotension, the hematologic events noted, hypoxemia, shock, or death.

The first patient to die was studied by the Armed Forces Institute of Pathology whose ". . . forensic environmental analyses at the AFIP (high-pressure liquid chromatography, gas chromatography and mass spectrometry) of the frozen sera samples were negative for volatiles and semi-volatiles including chloramines and carbon disulfide compounds."

The authors employed an inherently quantitative and elegant assay system but provided no quantitative result. If the samples or chromatograms had been preserved, it should have been possible to replicate the studies with standards sufficient to provide some quantitation of the sulfides they reported.

The authors dismissed positive blood cultures and endotoxin on the basis of the fever patterns, but the patients were elderly and uremic, two conditions that notoriously invalidate febrile responses. The patients' clinical courses were similar to those of patients receiving units of blood or other parenteral fluids contaminated with bacteria.

If the authors had found evidence that parenteral administration of the sulfides they implicated caused hypotension, hypoxemia, shock, leukocytosis with a profound left shift, toxic granulations, and Döhle bodies, such information would have strengthened their assertion of this being an example of sulfide lethal toxicity. A few animals observed after injection of these compounds would have been informative.

An alternative hypothesis is that the patients suffered from bacterial and endotoxin shock with classic systemic inflammatory response syndrome and that during the prolonged period of dialysis inactivity, as the authors stated, "in the anaerobic and septic environment" of the inactive reverse osmosis unit, "disulfides were likely produced by sulfate-reducing bacteria on the improperly maintained reverse osmosis unit membranes." This may have occurred long after the patient exposures and be unrelated to their symptoms, sepsis, shock, and deaths.

REFERENCE

1. Selenic D, Alvarado-Ramy F, Arduino M, et al. Epidemic parenteral exposure to volatile sulfur-containing compounds at a hemodialysis center. *Infect Control Hosp Epidemiol* 2004;25:256-261.

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The authors reply.

Dr. Thompson lists several symptoms and findings exhibited by case-patients, some of which are suggestive of infection, such as fever and hypotension. However, only some of the case-patients had any one of the findings on his list. For example, fever was present in only 4 of 16 case-patients.[1] The only findings exhibited by most case-patients were nonspecific in nature (eg, chills and nausea).

Dr. Thompson questions the laboratory analysis of samples related to the epidemic. He correctly implies the usefulness of quantitative data for volatile sulfur-containing compounds in water samples. Unfortunately, the emergency response nature of this investigation precluded the proper collection of water samples for later quantitation of volatiles. Additionally, solid-phase microextraction was used to extract the volatile sulfur-containing compounds for analysis. This method requires internal standards for adequate quantitation, and appropriate internal standards were not immediately available. The resulting water data were thus qualitative, not quantitative, in nature. Our previous experience with measuring volatiles in blood,[2] including carbon disulfide, led us not to attempt to measure volatile sulfur-containing compounds in blood samples collected from these patients. Significant quantities of sulfides contaminate blood collection tubes from the vulcanization process used to produce the butyl rubber stoppers, and thus compromise sulfide measurement in this matrix. Urinary metabolites of sulfides are effective biomarkers of exposure,[3] but urine samples were not available from this population. We responded to this emergency situation with the best methods available to our laboratory for generating timely results; the qualitative water data provided useful etiologic clues concerning this unfortunate epidemic.

Dr. Thompson advances the alternative hypothesis that "the patients suffered from bacterial and endotoxin shock," based in part on the belief that elderly and uremic patients will have a blunted febrile response. However, only two case-patients had positive blood cultures (for different organisms). Also, in several previously reported outbreaks linked to bacteremia and endotoxin, hemodialysis patients commonly exhibited a brisk febrile response.[4]

In our article, we concluded only that "Parenteral exposure to volatile sulfur-containing compounds . . . could have caused the outbreak." Although there is insufficient evidence to definitively implicate sulfites as the cause, there is good evidence against Dr. Thompson's hypothesis that bacterial infection was the cause.

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