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The authors reply.

Dr. Tietz and his associates state that the values in the figure do not correspond with statements in the text. In fact, they do. Although the lines of the graph may appear to reach zero in accordance with the statement by Dr. Tietz and his associates, in actuality, 10^5 *Pseudomonas aeruginosa* gave 2,135 RLUs, 10^6 *Escherichia coli* gave 1,369 RLUs, 10^3 *Candida albicans* gave 582 RLUs, and 10 red blood cells gave 14,274 RLUs. All were within the detectable range of the instrument. In addition to the quantitative data listed, quantitative studies were also performed with *Staphylococcus xylosus*, *Erysipelothrix rhusiopathiae*, *Enterococcus durans*, *Streptococcus bovis*, *Streptococcus pyogenes*, *Staphylococcus aureus*, and *Streptococcus pneumoniae*. Data from these studies were presented to the editor as a note in proof, but were omitted from the publication because they provided no additional significance to the data given.

We chose not to mislead readers into thinking that the bioluminescence assay is an exact quantitative measurement of colony-forming units. At least in our laboratory, we could not demonstrate precise quantitative numbers using this assay. The results we obtained for RLUs did, however, demonstrate approximate numbers of organisms on the logarithmic scale that best indicated high versus low microbial load.

The culture of endoscopes in this study included brushing the internal channels and the exterior of the endoscopes to dislodge any organisms. All were cultured or tested by gene probe technology. Therefore, the sampling for cultured endoscopes was the same as for the LUM-T assay with the exception that the entire internal channel was not sampled for the LUM-T assay. Five endoscopes that had negative results on the LUM-T assay were also cultured and had negative results. These five endoscopes served as the negative control, and if the sterile water used to rinse endoscopes had been contaminated, cultures would have revealed this. Therefore, the culture of the sterile water as suggested by Dr. Tietz and his associates is irrelevant.

We agree with Dr. Tietz and his associates that the cutoff values for sterile, clean, and contaminated were based on our observations, and we stated in the article that "other institutions may choose to set different limits based on their experiences with the LUM-T system."

High-level disinfection of endoscopes is a controversial issue. High-level disinfection does not equal sterility. Some argue that endoscopes should be rendered sterile and that only sterile endoscopes be used for patient care. Is this practical in the clinical setting?

Our findings showed that once endoscopes were reprocessed, they were not maintained in a sterile environment but rather a clean environment. Thus, our discussions with physicians indicated that some environmental contamination of endoscopes does reoccur prior to patient use. The level of recolonization then becomes a concern and an issue to be addressed. At what microbial load do we then deem an endoscope "improper for reuse?" How do we measure that in real time? Microbial culture of endoscopes requires days to weeks and is impractical. The bioluminescence assay can demonstrate contamination above that of normal skin flora and may prove to be the best rapid method available to demonstrate this phenomenon.

We have not stated or implied that a negative result on LUM-T assay equals sterility. The concept that not a single vegetative cell should exist on or inside the instrument before patient reuse is an idealistic one. We do not argue that conceptually sterility is the best practice, but rather that it is not the current standard. The question that then arises is whether it is feasible to create such standards. Unless standards are changed so that high-level disinfection imparts sterility and that sterility is maintained throughout storage and handling, we cannot ensure that infections will not arise from reprocessed endoscopes. Therefore, the decision to assume that all endoscopes are sterile because they have been high-level disinfected and to not monitor this process is misleading and possibly harmful.

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Epidemic Parenteral Exposure to Volatile Sulfur-Containing Compounds at a Hemodialysis Center

To the Editor:

In the March issue of *Infection Control and Hospital Epidemiology*, Selenic et al. reported that an epidemic became manifest during 30 minutes beginning approximately 1 hour after reverse osmosis units were returned to the treatment loop during dialysis of 16 patients.[1] Their symptoms included chills, nausea, vomiting, hypotension, hypoxemia, tachypnea, fever, leukopenia followed by leukocytosis with a profound left shift, toxic granulations, and Döhle bodies. Two patients died and two had positive blood cultures, one for *Citrobacter*. Some water samples at the site contained excess endotoxin, and others contained excess viable aerobic bacteria.

The authors obtained samples 6 days after the dialysis center had been closed and the reverse osmosis unit had been sitting without water circulation. A "sulfur" odor was detected, which had been noted only once previously by an attendant, and the presence of four sulfur compounds, which the authors note may have been generated by growth of anaerobic bacteria in the inactive reverse osmosis unit, was detected by gas chromatography and mass spectrometry.

The authors stated that this was the first reported hemodialysis outbreak linked to sulfide exposure. They reviewed the toxicology of the sulfides they detected, given by non-

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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