

## CORRESPONDENCE

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## Renal Cysteine Conjugate $\beta$ -lyase and Compound A Nephrotoxicity: Minimal Evidence for an Association

*To the Editor:*—We are writing to you with regards to the manuscript published in the June 1998 issue of ANESTHESIOLOGY titled, "The Role of Renal Cysteine Conjugate  $\beta$ -lyase Pathway in Inhaled Compound A Nephrotoxicity."<sup>1</sup> The major theme of this article is that compound A-induced nephrotoxicity, produced by either intraperitoneal or inhalation routes of administration, is dependent on the metabolism of cysteine conjugates of compound A by renal cysteine conjugate  $\beta$ -lyase. After careful reading of this paper, it became apparent to us that the article is very misleading, because it contains several instances in which the authors have made statements that are inconsistent with the results, not only of their study, but also those of previously published articles. Although, there are several inconsistencies in the discussion of the manuscript, the abstract is a good place to focus our commentary, because it is often the only section of an article that is read, and it contains most of the misleading statements.

In the background section of the abstract, the authors state that it was previously shown that aminooxyacetic acid diminished the nephrotoxicity of intraperitoneally administered compound A; however, the article published in ANESTHESIOLOGY, January 1997, clearly showed that aminooxyacetic acid did not inhibit compound A-mediated renal necrosis or glucosuria, a finding suggesting that pathways of metabolism other than that mediated by renal cysteine conjugate  $\beta$ -lyase contributed to the nephrotoxicity of compound A.

The authors claim in the results section of the abstract that "probenecid diminished ( $P < 0.05$ ) compound A-induced glucosuria." Figure 3, however, shows that there was no statistical significance assigned to this effect. The authors state that aminooxyacetic acid decreased compound A-dependent proteinuria and glucosuria; yet figure 4 shows that these decreases were not statistically significant, a further finding that is not consistent with compound A-induced nephrotoxicity being mediated by the renal cysteine conjugate  $\beta$ -lyase pathway of metabolism. Moreover, the authors purport that "aminobenzotriazole had no consistent effect on the nephrotoxicity of compound A," which seems to suggest that the cytochrome P450 metabolism of compound A or its metabolites, or both, does not have a role in compound A-induced nephrotoxicity. Nevertheless, the manuscript actually shows that the

preadministration of this cytochrome P450 inhibitor significantly decreased the histologic necrosis (table 1) and rise in BUN (table 2) caused by Compound A, indicating that cytochrome P450-mediated metabolism may have a role in compound A-induced nephrotoxicity.

In the conclusions section of the abstract, the authors leave the readers again with the notion that their findings implicate the role of renal cysteine conjugate  $\beta$ -lyase in compound A-induced nephrotoxicity, even though their results are not consistent with this idea.

In conclusion, it is disturbing that this article contains this many discrepancies that are misleading. Maybe it is no longer prudent to rely on reading only abstracts.

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## Reference

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*In Reply:*—Drs. Njoku, Pohl, and Martin state that our article<sup>1</sup> is "very misleading, contains statements inconsistent with the results and those of previously published articles, and contains discrepancies that are misleading." We disagree and believe they misrepresent the paper and its predecessor.<sup>2</sup> Drs. Njoku, Pohl, and Martin apparently do not

disagree with the fundamental conclusion of the investigation, that compound A effects appear similar whether it is administered by inhalation or intraperitoneal injection. Rather, they criticize wording in the abstract, which was restricted by ANESTHESIOLOGY to 250 words.

For example, we summarized<sup>1</sup> our previous<sup>2</sup> results, that probenecid