

## Serum Selenium in Lymphoma

**TO THE EDITOR:** We read with interest the paper by Last et al<sup>1</sup> in a recent issue of *Journal of Clinical Oncology*. The authors observed that serum selenium concentration at presentation predicted for dose delivery, response to therapy, and long-term survival in patients with aggressive non-Hodgkin's lymphoma (NHL). They speculate that the underlying mechanisms may include prevention of chemoresistance, enhancement of immune function, cytotoxic activity of selenium compounds, and reduction of chemotherapy side effects. They also allude to the possibility that low serum selenium could just be a marker of general nutritional deficiency or an acute phase reactant. However, the authors failed to consider another important possibility; that is, that selenium concentration could be a marker of disease proliferation. From our own data published approximately 15 years ago, we think that this is the most likely explanation.

In the first study, we measured serum trace elements in small groups of patients with various hematologic malignancies.<sup>2</sup> Although serum selenium was normal in patients with multiple myeloma, chronic lymphocytic leukemia (CLL), and myeloproliferative disorders, it was apparently decreased in those with Hodgkin's lymphoma or non-Hodgkin's lymphoma (not significant). This was later confirmed by others.<sup>3</sup> We then carried out a more detailed study in 50 patients with CLL and 100 normal participants.<sup>4</sup> Although serum selenium was similar overall in CLL patients compared with levels in the controls, levels were significantly lower in Rai stages 3 to 4 compared to Rai stages 0 to 2 ( $0.079 \pm 0.011$  v  $0.108 \pm 0.006$   $\mu\text{g/mL}$ ;  $P = .0390$ ). In addition, serum selenium correlated negatively ( $P < .05$ ) with the lymphocyte count in patients with more than  $20 \times 10^9/\text{L}$  lymphocytes. Therefore, serum selenium seemed to be related to the extent of the disease. However, we emphasized that we could not determine whether differences in selenium levels were responsible for or caused by tumor proliferation. In a final study, serum selenium levels were measured before, during, and after high-dose induction chemotherapy in 70 patients with acute myelogenous leukemia (AML).<sup>5</sup> Pretreatment serum selenium levels were lower in patients than in controls ( $0.082 \pm 0.033$  v  $0.097 \pm 0.035$   $\mu\text{g/mL}$ ;  $P < .01$ ) and correlated inversely with the absolute peripheral blast cell count ( $P < .001$ ) and other measures of the tumor burden. After 7 days of chemotherapy, selenium increased significantly in proportion to the initial tumor burden ( $P < .01$ ). Thereafter, serum selenium levels remained normal in patients entering a

complete remission, whereas levels gradually decreased to baseline values in patients who experienced treatment failure. These data do not lend support to the hypothesis that a low selenium status enhances the risk of developing AML, but indicate that serum selenium levels in patients with AML are mostly dependent on tumor activity.

In view of the close relationship with tumor burden and the rapid modifications induced by chemotherapy, a mechanism of selenium sequestration by tumor cells is possible. Some evidence that certain tumors can accumulate selenium has been reported.<sup>6</sup> In their article, Last et al indicate that performance status was the only clinical variable correlating with selenium concentration, but they do not show any data on such associations with stage, serum lactate dehydrogenase, International Prognostic Index, tumor masses, or other factors. In addition, follow-up measurements during chemotherapy would have been most useful.

Contrary to the conclusions of the authors, we believe that until all these aspects of selenium metabolism in lymphoma patients are clearly sorted out, incorporation of selenium supplementation into an overall therapeutic strategy is not warranted. It could even have some unforeseen deleterious effects on outcome.

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### Authors' Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.

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