The authors reply:

To the Editor: Moos gives an obvious and apparently simple solution for my riddle regarding bel-6 rearrangements in large-cell lymphoma. In fact, the issue he raises is semantic, because the in vivo behavior of a tumor and the prognosis for the patient can only be determined in relation to what is known about other tumors and other patients. My suggestion that rearrangement of bel-6 in large-cell lymphoma "apparently curtails the malignant behavior of the tumor" does not necessarily relate to the early steps in oncogenesis; it could be that the rearrangement induces a phenotype that inhibits other genetic events or the expression of other oncogenes. Alternatively, expression of the bel-6 gene may directly or indirectly enhance the sensitivity of the tumor to cytotoxic drugs.

Several arguments suggest that rearrangement of bel-6 has a positive influence on prognosis. In the series of Offit et al., patients with large-cell lymphomas who harbored a rearrangement of bel-6 had an excellent prognosis, with a projected survival of 91 percent and a projected rate of freedom from disease of 82 percent at 36 months. This result, remarkable for a very heterogeneous disorder with multiple prognostic factors, points to a "common" genetic factor.

Moos suggests that other genetic abnormalities may cause the poor prognosis in patients with large-cell lymphomas lacking a bel-6 rearrangement. Offit et al. studied this possibility with regard to the two most common oncogenes, bcl-2 and nyc. Rearrangements of these genes were not independently related to prognosis. Thus, according to Moos, there should be as yet unidentified genetic events. Bastert et al. found that almost all lymphomas with a rearrangement of band 3q27 had complex cytogenetic abnormalities. Generally, complex karyotypes are associated with an adverse prognosis. Although the series of Bastert and Offit differ, this suggests a beneficial prognostic factor in Offit's group of large-cell lymphomas with rearrangement of bel-6.

It is not unprecedented to propose that the activation of an oncogene may confer a certain disadvantage to the tumor. In Burkitt's lymphoma, activation of nyc by t(8;14) is a prerequisite for tumorigenesis; at the cellular level, nyc enhances cell proliferation and blocks differentiation. On the other hand, nyc also induces apoptosis of tumor cells, which might be regarded as a disadvantage.2,3

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To the Author: Dr. Moos's hypothesis is consistent with an analysis of the subgroup of 65 karyotypically abnormal large-cell lymphomas in our series.1 Karyotypic complexity, as measured by the mean number of marker chromosomes (M), calculated as described elsewhere,2 was greater for the group with germ-line bel-6 (M = 6.1) than for the group with bel-6 rearrangement (M = 4.1, P = 0.01). This suggests that the germ-line group may have had additional genetic abnormalities, some of which were associated with progression and poor clinical outcome.3

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To the Editor: With regard to Dr. Lynch's discussion (July 14 issue) of the case of a 41-year-old woman with a lytic jaw mass, lymphadenopathy, splenomegaly, and a multifocal neurologic disorder, the patient's reports of numbness and impaired sensation on the right side of the chin is typical of temporal neuropathy, also known as the numb chin syndrome. This clinical presentation, combined with the finding of a lytic jaw lesion, suggests that the chin numbness resulted from local involvement of the inferior alveolar nerve or the mental nerve.

This uncommon cranial neuropathy is mostly associated with neoplastic disorders.2 Its appearance in a 41-year-old woman with no history of smoking should have directed the evaluation toward metastatic breast cancer or high-grade malignant lymphoma, the two most common causes of the syndrome. Among the lymphomas, the numb chin syndrome occurs with notable frequency in American Burkitt's lymphoma and Burkitt's-cell acute lymphoblastic leukemia, providing an additional clue to the diagnosis.

Chin numbness may occur at presentation or with systemic dissemination of the basic disease. Its most frequent causes are compression of the mental nerve or the inferior alveolar nerve by jaw metastases and intracranial involvement of the mandibular nerve by lesions at the base of the skull. Lymphoproliferative and myeloid malignancies may also cause chin numbness and should be excluded in patients with multifocal neurologic involvement, as was done in this case. Thus, we believe that the patient's presentation with the numb chin syndrome was highly suggestive of the presence of neoplastic disease, most likely a high-grade lymphoma.

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To the Editor: The numb chin syndrome typically occurs in patients with lymphoma, especially Burkitt's lymphoma, and is associated with a poor prognosis. The numb chin syndrome is characterized by numbness and paresthesias in the lower lip and chin, and is often associated with jaw metastases. The numb chin syndrome is usually seen in patients with advanced-stage disease and is a poor prognostic indicator.

CASE 27-1994: THE NUMB CHIN SYNDROME

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