

spect to the relation between κ or λ L-chains and response to therapy. We have not been able to find any clue through analysis of the abnormal myeloma proteins to help us predict survival time or response to therapy of any kind.

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In our report we said, "The concept that tumor-cell differentiation may influence the response to chemotherapy needs to be explored further, and considered in future therapeutic trials in myeloma." We were, in effect, asking other investigators to review their data and to plan future studies to confirm, or refute, our findings. Therefore, although we are a little deflated, we welcome the letters of Osserman and of Lee *et al.* The recording of objective improvement in five of ten patients producing only λ -BJP and of the failure of three of six patients producing only κ -BJP to improve following melphalan therapy certainly presents a different frequency of response from what we have reported. These data clearly indicate that the correlation of melphalan response to these proteins types is not absolute; but they are still inadequate to disprove the thesis that patients producing only κ -BJP respond more frequently than those producing only λ -BJP.

The differences in the frequency of response to melphalan observed by Osserman, Lee *et al.*, and by the Southwest Cancer Chemotherapy Study Group (SWCCSG) may be due to many factors, so that it is difficult to compare the three series. Two important differences are the dosage schedules employed and the selection of evaluable patients. Osserman only evaluated the response of patients treated for 6 months or more, and Lee *et al.* report on "adequately treated" patients (27 of 40) observed on therapy for a minimum of 3 months, whereas we evaluated the response of all patients followed for at least 3 weeks. We found that 6 to 9 months of treatment were required for optimum improvement, but in most cases it was possible to rate the response within 3 weeks after the first course of the drug (1.0 mg/kg in 4 days). In

our series, 14 of the total group of 91 (15.4 percent), 2 of 12 patients (16.6 percent) producing only κ -BJP, and 3 of 9 patients (33.3 percent) producing only λ -BJP, died within the first 6 months. The elimination of patients who die early would probably result in the loss of more nonresponders than responders from the series of Osserman and of Lee *et al.*; this makes their series different from ours.

Osserman suggests that the excessive toxicity of our melphalan dosage schedule A may have contributed to our poor results with patients producing only λ -BJP. This is very unlikely; none of the patients treated with schedule A or B died as a result of hematological toxicity, and all of the patients excreting only κ - and λ -BJP were treated with schedule B. The mean melphalan dose rate (mg/kg/month) was 0.59 for the κ -BJP group and 0.53 for the λ -BJP group; these dose rates are not significantly different.

Even if we assume that the different melphalan dosage schedules employed by Osserman, Lee *et al.*, and the SWCCSG did not influence the results, and also assume that there were no early deaths in the Osserman or Lee *et al.* series, there is still convincing evidence that patients producing only κ -BJP respond more frequently (14 of 17) than those producing only λ -BJP (5 of 19), when the results of the three series are combined.

We believe that a well-designed prospective study, with a larger number of patients, will be required to confirm or refute our report, for the patients should be unselected and treated in a comparable fashion, and the results should be analyzed carefully from many points of view. Different dosage schedules should be tested to determine whether this factor influences the frequency of response. These studies will require a protocol.

The last paragraph of Osserman's letter is most disturbing, for it implies that a rigid protocol interferes with the proper medical management of patients. If this were the case, cooperative group studies would be unethical. The SWCCSG and other cooperative study groups take great care to emphasize optimum supportive care in addition to the study drug. The protocols employed are rigid only in the sense that the study plan must be such that the effectiveness of the study drug or dosage schedule can be evaluated; it is inconceivable that a

study protocol would prevent investigators from using the important supportive measures mentioned in Osserman's letter. We have found that patients are investigated more completely, seen more frequently, and probably receive more enlightened general care now than they did before study protocols were introduced into our institutions.

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Changes in the Tail Feathers of the Adolescent Lyrebird

Since the publication of my report on the changes which occur in the tail feathers of the adolescent lyrebird, *Menura superba* [*Science* **147**, 510 (1965)], evidence has been obtained which renders it necessary to correct a statement on page 512 (near the top of column 2) of that report regarding the development of the two central feathers (medians). It is now clear that these feathers progress from the juvenile to the mature form by a series of moults and replacements and not by transformation of the juvenile vaned feathers into the adolescent medians.

It is also apparent that the other vaned feathers undergo changes in form (by moulting and replacement) as the bird matures. Recently the almost complete tails were recovered from two birds which had been killed by predators. One bird was in its first or early in its second year, while the other was in its third or fourth year. Though one of the medians was broken, the differences between the plain feathers and between the medians of the two birds are clearly visible. Photographs are available.

The filamentation process whereby plain vaned feathers are converted into or replaced by filamentaries, which was described in the previous report, begins at a later stage.

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