To the Editor:

We are pleased that Drs Venook, Shuman, and Corash concur with our conclusion that the benefit of prophylactic heparin in the management of acute promyelocytic leukemia (APL) is presently unproven. Furthermore, we are glad that they share our stated concerns over the use of historical controls and that they concur with our final recommendation that a prospective, randomized trial would be required to determine the optimal means of providing supportive care for patients with APL. We take serious exception, however, to the implication that our analysis of previous studies was basically flawed. The data attributed to Cunningham and colleagues were based on updated figures kindly provided to us in a personal communication; perhaps the data should have been referenced as such. With regard to the report by Kantarjian and co-workers, we stand technically corrected in that 13 of the 60 patients did not receive an anthracycline but rather were treated with amascrine. Our purpose in attempting to limit our analysis to anthracycline-based regimens was to focus our analysis on somewhat more contemporary, intensive chemotherapeutic regimens in an effort to avoid potentially problematic comparisons with older historical controls. The inclusion of the amascrine-based regimens of Kantarjian and colleagues conforms with this reasoning since they are intensive regimens and have been shown to have efficacy similar to that of anthracycline-based regimens. We wanted to exclude less comparable, less intensive regimens such as the drug combination given to seven of the patients of Drapkin and colleagues between 1970 and 1973 (included in Table 1 of Venook et al.). Even taking into account these trivial changes in the data of Cunningham and colleagues and Drapkin and associates, however, and including all of the data from Kantarjian and co-workers, we still obtain a hemorrhagic death rate of 20% (35 of 175) in patients treated with heparin and 29% (36 of 124) in patients not receiving heparin. This is not significantly different from the hemorrhage-related death rate of 19% (34 of 179) in heparin-treated patients and 28% (33 of 117) in patients not receiving heparin reported in our article.

The only significant change in interpretation of previous studies which Venook and colleagues apparently wish to make is in the study of our patients had DIC initially or shortly after beginning induction therapy. This is comparable to many previously reported series and does not appear to reflect a population of patients with a lesser bleeding diathesis.

Finally, the main point of our article was to make clear that although heparin is accepted as a standard method of practice, it has not been shown to be a necessary component in the treatment of APL. In our experience, the coagulopathy associated with APL can be successfully managed with intensive chemotherapy and blood product support without routine use of heparin. We believe it is contrary to the usual practice of medicine to adopt a potentially toxic therapy prior to demonstrating its benefit.

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REFERENCES


DISTRIBUTION OF TRANSFERRIN RECEPTORS IN THE CELLULAR COMPONENTS OF THE LIVER

To the Editor:

The recent work by Vogel et al., demonstrating the presence of transferrin receptors in nonparenchymal cells of the liver, is interesting and very much in line with our own published work.

Regrettably, however, this recent work is subject to the same criticism that the earlier works by Young and Aisen were. The basic assumption in kinetic studies of receptor-ligand interaction using radiolabeled ligand is that the cell population under study is homogeneous. This is because in all calculations the denominator is the number of cells. Clearly, if a proportion of cells have a certain type of receptor and others do not, calculation of affinity, maximum binding, and number of receptors per cell would be erroneous. The earlier work by Young and Aisen was subject to this criticism because they used crude liver cell suspensions (a mixture of parenchymal and nonparenchymal cells) and attributed all the binding to parenchymal cells. Although Vogel et al fractionated parenchymal cells, they treat nonparenchymal cells as if they were a homogeneous cell population; they are not. They contain both Kupffer cells and endothelial cells. The latter cells, not the former as we have demonstrated, possess transferrin receptors. The heterogeneity of this cell population invalidates results obtained by the application of the radiolabeled ligand binding assay.
Distribution of transferrin receptors in the cellular components of the liver [letter]

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