from a sequential blockade in thymidylate synthesis or as a form of concurrent blockade involving purine and thymidylate biosynthesis. However, although therapeutic enhancement was obtained with the combination, it was concluded that the fundamental nature of the enhanced therapeutic response remained to be determined. Thus, although in accordance with the rationale, an "expected drug interaction" occurred, the fundamental basis for the therapeutic enhancement may not have been related at all to this interaction.

A wide variety of combinations of drugs has been demonstrated, in animal tumor systems, to provide a therapeutic advantage over that observed with the drugs employed individually. The demonstration of such therapeutic synergism may be dependent upon the dosage ratios employed, the dosage levels, and the schedule of administration, including the interval between treatments, number of treatments, total duration of treatment, and the timing of administration of the drugs relative to one another. The degree of advancement of disease and extent of infiltration or metastasis, as well as a variety of factors pertaining to the host, may influence the extent of therapeutic effect observed. Any biochemical rationale pertaining to fundamental interactions of a drug combination must be reflected in increased antitumor specificity in the tumorous host in order to obtain an improved therapeutic response.

We agree with Maugh that detailed investigations of drug combinations should be conducted and that fundamental investigations of biochemical and pharmacologic action, both in vitro and in vivo should be pursued, both retrospectively and prospectively, in relation to the usefulness of drug combinations in the treatment of clinical neoplasia.

ABRAHAM GOLDIN

Division of Cancer Treatment, National Cancer Institute, Bethesda, Maryland 20014

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1. I. Kline, J. M. Venditti, J. A. R. Mead, D. D. Tyrer, A. Goldin, *Cancer Res.* **26**, 848 (1966).
2. I. Kline, J. M. Venditti, M. Gang, A. Goldin, unpublished data.

Mailing Labels: Hot Air, Patience, and Other Suggestions

Eugene E. Hinman (Letters, 12 Nov., p. 674) may remove the labels from *Science* covers by the application of heat from a hot air blower (a small hair dryer works very nicely) for about 15 seconds and then carefully peeling off the label. A hot iron will probably work equally as well, but water will not work, since the glue used on the label is not water-soluble. The heat treatment process produces a *Science* cover in mint condition, provided the Postal Service has not already mutilated it.

GARY THOM

Department of Chemistry, American University, Washington, D.C. 20016

. . . The mailing label can, in fact, be removed with spit and a little patience, though one has to be careful not to dig into the surface of the picture. Somebody (presumably the Postal Service) attaches circular colored stickers to the front cover. These, however, are easily peeled off without damage to the magazine. Perhaps the adhesive used for these stickers could be used also for the mailing labels.

R. JOHN STEDMAN

Department of Medicinal Chemistry, Health Sciences Center, School of Pharmacy, Temple University, Philadelphia, Pennsylvania 19140

. . . Would a double cover be a cheap solution to Hinman's problem?

K. B. FREEMAN

Department of Biochemistry, Health Sciences Centre, McMaster University, Hamilton, Ontario, Canada L85 4J9

. . . Simply place a plain wrapping paper cover over the formal cover, not as a wrapper but as an outside cover sheet, stapled with the rest of the sheets of the magazine. Print it with the title, so as to meet postal regulations, and put the mailing label on it.

ROBERT M. HAYES

Graduate School of Library and Information Science, University of California, Los Angeles 90024

. . . Perhaps, where possible, cover photos could be cropped so that the leftmost 15 percent contained no useful information. Otherwise, a smaller photo seems preferable to one that is flawed.

JOHN GRAHAM

Box 122, Guernewood Park, California 95446

. . . Why not reduce the cover illustration by 12 percent, place the label on the free space at the fold, and preserve the design intact for the reader to use and enjoy?

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