troscopist. I must accept their main point: at present one cannot analyze directly down to a concentration of 10^{-12} for a wide range of elements in biological materials.

In extenuation, it should be noted not only that Table 1 in my article was characterized in the text as quite approximate but that the entry for mass spectroscopy posed a special problem. For most of the methods listed in Table 1 I drew on performance figures achieved during extensive biological research. For mass spectroscopy there is no comparable literature, and the technique has not had the benefit of comparable intensive biological trial. The inherent sensitivity of the method would be obscured by listing limits representing the present degree of mastery of contamination. I tried, rather, to tabulate the outstanding inherent sensitivity, leaving the implication that the method should play a larger role in biological trace work. This implication seems to be confirmed by the remarks of Herzog and Marshall.

May I add a few brief comments. I did not refer to commercial instruments, and I did not mean to imply that the isotope dilution method of mass spectroscopy (with its approximately 68 suitable isotopes) was the only method suitable for trace work.

I cannot quite agree with Herzog and Marshall's comment on nondestructive analysis. One hopes to analyze identified microentities; hence, much of the advantage of nondestructiveness is generally lost if the unconsumed and the analyzed regions are not identical. The degree of destructiveness of the electron microprobe is not yet established, but even if it destroys a circular area 1 micron in diameter, with the surroundings remaining recognizable, I believe conventional mass spectroscopy cannot hope to match it in nondestructiveness. Of course, mass spectroscopy with a microfocused ion beam could conceivably be similarly nondestructive.

With respect to "blind spots" I should mention that several laboratories are now seeking intensively to extend x-ray spectroscopy down to atomic number 6.

In summary, I think that the exposition by Herzog and Marshall should be stimulating to trace-element biologists, and I hope we may have even more detailed evaluations of the capabilities of the mass spectrometric method.

At this point I would like to make amends for an unrelated omission in my recent article: With respect to zinc concentrations in malignant prostatic tissue, although I did not seek to give a comprehensive bibliography, I should have listed a relatively early work, "The occurrence of zinc in the human prostate gland," by C. A. Mawson and M. I. Fischer [*Can. J. Med. Sci.* **30**, 336 (1952)].

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Sparing of Folinic Acid by Thymidine

In the recent report "Sparing of folinic acid by thymidine," by Grossowicz and Mandelbaum (*1*), it is quite clear that several important literature references are lacking.

The synergistic action of folinic acid and thymidine in stimulating the growth of *Pediococcus cerevisiae (Leuconostoc citrovorum)* ATCC 8081 was first noted by Bardos *et al.* (*2*). Furthermore, the finding that thymidine increased the

growth of *P. cerevisiae* in the presence of high concentrations of pteroylglutamic acid (folic acid) was originally made by Broquist *et al.* (*3*).

The sparing of folinic acid by thymidine has interested several authors. Broquist *et al.* published a figure on this phenomenon (*4*, p. 402, Fig. 2), although a concentrate from liver was used as a source of folinic acid. A most thorough investigation on this subject has been published by Ellison and Hutchinson (*5*, p. 467); in their report both "the sparing effect of thymidine on the response of *P. cerevisiae* to citrovorum factor" (*5*, p. 473, Fig. 4) and "the sparing effect of citrovorum factor on the response of *P. cerevisiae* to thymidine" (*5*, p. 473, Fig. 5) are given. Review articles have also mentioned that thymidine will reduce the requirement of *P. cerevisiae* for folinic acid, a finding which is of importance in the assay for folinic acid of natural materials containing thymidine (*6, 7*).

In connection with studies of the synergistic growth effects on *P. cerevisiae* of folinic acid plus thymidine and of folic acid plus thymidine, the effect of folinic acid plus folic acid is also of interest. This has been investigated by Hendlin *et al.* (*8*), who found that media supplemented with subminimal levels of folic acid or N^{10}-formyl folic acid (rhizopteringlutamate) gave a threefold to fourfold increase in the response of *P. cerevisiae* to folinic acid.

Another interesting finding concerning *P. cerevisiae* is the growth-inhibiting effect of deoxyuridine noted by Bolinder and Kurz (*9*). The growth-promoting effect of suboptimal amounts of folinic acid (leucovorin) was inhibited noncompetitively by deoxyuridine. However, the growth-promoting effect of suboptimal amounts of thymidine (0.1 to 3 μg per 10-ml tube) was competitively inhibited by deoxyuridine, and an inhibition index of about 30 was obtained after 48 hours of incubation at 37°C. No inhibition occurred when leucovorin or thymidine were present in amounts sufficient to promote optimal growth of *P. cerevisiae*.

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References

1. N. Grossowicz and F. Mandelbaum, *Science* **133**, 1773 (1961).
2. T. J. Bardos *et al.*, *J. Am. Chem. Soc.* **71**, 3852 (1949).
3. H. P. Broquist *et al.*, *Proc. Soc. Exptl. Biol. Med.* **71**, 549 (1949).
4. H. P. Broquist, E. L. R. Stokstad, T. H. Jukes, *J. Biol. Chem.* **185**, 399 (1950.).
5. R. R. Ellison and D. J. Hutchison, in *The Leukemias*, J. W. Rebuck, F. H. Bethell, R. W. Monto, Eds. (Academic Press, New York, 1957).
6. R. P. Tittsler *et al.*, *Bacteriol. Revs.* **16**, 246 (1952).
7. R. H. Girdwood, in *Advances in Clinical Chemistry*, H. Sobotka and C. P. Steward, Eds. (Academic Press, New York, 1960), vol. 3, p. 272.
8. D. Hendlin, L. K. Koditschek, M. H. Soars, *J. Bacteriol.* **65**, 466 (1953).
9. A. E. Bolinder and W. G. Kurz, *Acta Chem. Scand.* **13**, 2160 (1959).

I am embarrassed about not having seen the paper of Broquist *et al.* (*1*) prior to submitting our report for publication. Bolinder is certainly justified in bringing the information to light; however, I consider that he makes too much of an issue of it. I believe I have good knowledge of the literature, although it is quite difficult nowadays to keep up with all the published works in a given field. With reference to this subject, I have corresponded with some of the workers in the field, asking for their interpretations of the differences in the results obtained. Moreover, I showed our results to E. L. R. Stokstad, a coauthor of Broquist's (*1*), and he did not mention having obtained results similar to ours some 10 years ago.

My failure to see the article of Broquist (Bolinder's references *2*, *5*, and

6 are much less relevant) is due to the fact that it dealt with different aspects of folic acid (the title is "Some biological and chemical properties of the citrovorum factor") and therefore slipped my attention. I learned about the synergistic effect of folinic acid and thymidine from the recent review of Girdwood (*2*). This was, however, after our article had already been printed.

In retrospect I feel that our "rediscovery" of the sparing of folinic acid by thymidine served a good purpose, as many workers, like ourselves, did not know about the previous publication. I base this statement on the fact that there is quite a demand for reprints of our article. Thus, in spite of oversight on my part, our paper served to disseminate useful scientific information.

I feel that if *Science* as well as other journals would put more emphasis on the importance of identifying articles by proper headings, a slip of this sort would become a rarity.

With regard to the information presented in our report I would like to emphasize that in addition to the phenomenon of synergism, our findings demonstrate for the first time the quantitative aspects of the effect with pure compounds (the chemical authenticity of "folinic acid" was not established in the articles of Broquist *et al.* and the others). Moreover, in our system thymidine alone is ineffective, while it produced growth in their experiments (Bolinder's references *2* and *3*).

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References

1. H. P. Broquist, E. L. R. Stokstad, T. H. Jukes, *J. Biol. Chem.* **185**, 399 (1950).
2. R. H. Girdwood, in *Advances in Clinical Chemistry*, H. Sobotka and C. P. Stewart, Eds. (Academic Press, New York, 1960), vol. 3, p. 235.

Migrant Asian Students

The influx in recent years of Asian students in our universities has often presented problems of adjustment, owing perhaps as much to inadequately informed advisers as to the radically new cultural and academic patterns facing many of these students. Counselors of graduate students and, more especially, faculty members involved in educational exchange programs may on rare occasions have failed to notice