proceeding on schedule with the assistance and approval of the Department of Agriculture.

In a more general vein, nutrition research has indeed been moved as part of the overall reorganization of the Department of Agriculture. It will now be more closely integrated with agricultural research, thus assuring nutrition a central place in the Department's programs.

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Malathion Safety Record

Jean L. Marx's article "Malathion threat debunked" (Research News, 31 July, p. 526) does not mention the massive and successful aerial spraying of south Florida in 1956 to eradicate the Mediterranean fruit fly—a highly sophisticated operation with protective measures for beehives, fish farms, auto painters, and so forth that should be a model for the California program.

There has been no indication of any health hazard whatsoever as a result of this heavy application of malathion, the spraying in 1962–1963 over three counties, and the continued use of malathion for mosquito control. Because of this safety record, Florida experts advised aerial spraying in California 8 or 9 months ago. If heeded, there would be no crisis nor health-hazard furor today.

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Saccharin and Bladder Tumors

Several reports (*1*) suggest an increased incidence of bladder tumors in male rats fed high doses of saccharin for prolonged time intervals. These reports review the information on saccharin which indicates that very little, if any, is metabolically altered and that the compound is essentially completely eliminated in the urine. The compound does not appear to react with DNA, and its mutagenicity is debatable. The mechanism by which an otherwise innocuous compound can induce bladder tumors appears to be an enigma. We should like to suggest a factor which appears to have been overlooked.

The bladder tumors are seen only with maximum tolerated doses of sodium saccharin which are in the range of 4 grams per kilogram per day. Since all of this would appear in the urine, which may be estimated at a volume of 200 milliliters per kilogram per day, the concentration of saccharin in the urine of these rats would be approximately 0.1 molar. Saccharin, however, is an acid with a pK_a of about 1.4 (*2*) and therefore should be distributed across cellular membranes according to the *p*H gradients across those membranes. The *p*H of the rats' urine was about 6.0; indeed, in the studies cited ammonium chloride (NH_4Cl) was administered to some of the rats to maintain the urine at an acid *p*H value. Although the intracellular *p*H of rat bladder epithelium is not known, most mammalian cells have an intracellular *p*H of about 7.0 (*3*), and it is reasonable to assume that bladder epithelial intracellular *p*H should be near this value. Furthermore, NH_4Cl treatment can raise intracellular *p*H due to the transmembrane diffusion of nonionized NH_3. Therefore, at a urine *p*H of 6 and an intracellular *p*H of at least 7, the intracellular concentration of saccharin in the bladder epithelium should be greater than 1 molar. This concentration approaches the solubility limit for some salts of saccharin. Even if intracellular precipitation of saccharin salts does not occur, the effect of such a massive solute concentration on cellular functions must be profound. The chronic physical presence of these high concentrations of saccharin ions precipitates, or both, might induce tumors through an indirect effect on the cells' internal environment. Therefore, the tumors may be an artifact of the combination of massive doses, renal elimination, and cellular transmembrane *p*H gradients in the bladder.

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Erratum: In the report "Staining of blue-sensitive cones of the macaque retina by a fluorescent dye" by F. M. de Monasterio *et al.* (11 Sept., p. 1279), the calibration bar, referred to in the legend of Fig. 2, was omitted; the bar corresponds to 5 mm of the printed page. In the same report, the labeling of Fig. 3C (bottom right panel of Fig. 3, p. 1280) is missing. Its ordinate axis should read "Percentage," and the ordinate axis marks should read (from top to bottom) "13, 11, 9, 7, 5."

Erratum: The mezzotint of Isaac Newton on page 1341 of the issue of 18 September should have been credited to the Prints Collection, New York Public Library, by permission of New Republic Books.