LETTERS

Small amounts

D. CHAKRABORTI

A report about possible "increase in potency of weakly estrogenic compounds when used in combination" is said to have "aroused considerable interest." One physician's early diagnosis and reporting of arsenic poisoning from well water in India—and the wider response to the problem—are described. (Right, a bicycle brigade of patients/data collectors in West Bengal.) A Mayan mural might depict "some species of blue macaw." Organisms as small as 0.01 micrometer in diameter may exert "an enormous influence on Earth's surface chemistry." And an "impressive" experiment using two marbles is proposed.

Activation of Estrogen Receptors

The report by S. F. Arnold *et al.* (7 June, p. 1489) demonstrating an increase in potency of weakly estrogenic compounds when used in combination has aroused considerable interest. A number of aspects of the report, however, are unclear.

First, the chemicals that were used (the pesticides endosulfan, dieldrin, toxaphene, and chlordane) are not the most obvious choice: for example, Sharpe *et al.* used 4-octylphenol and butyl benzyl phthalate in their demonstration of reproductive effects in rats (*1*). Second, in the latter part of the report, concerning human endometrial cancer cells, the focus switches to an interaction between two polychlorinated biphenyls (PCBs), rather than sticking with the same pesticides. In neither case is a justification given for the selection or rejection of compounds in the study's design.

Third, the significance of the findings is unclear: even the potentiated action is less than that of estradiol by a factor of 10^3. Fourth, the results of one of the tests used, inhibition of estradiol binding, could equally well correspond to an estrogenic antagonistic as to an agonist effect in vivo.

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Response: Joffe inquires about the selection of the compounds used in our study of the synergistic action of weakly estrogenic chemicals. The pesticides (endosulfan and others) were chosen because they had been shown to function individually as estrogens in mammalian cells and to stimulate greater-than-additive responses when combined (*1*). The hydroxylated-PCB-stimulated estrogen-specific responses in mice (*2*) and turtles (*3*), and a combination of the two hydroxylated PCBs produced synergistic responses in the turtle (*3*). The pesticides and the PCBs interacted with the estrogen receptor in competitive binding assays, suggesting that the estrogenic activity observed was occurring at the level of the receptor (*1*, *2*).

Another factor in the selection of the compounds that we did not present in our original report was mentioned in another paper (*4*). The pesticides tested in our study, and related PCBs, were identified in alligator eggs from Lake Apopka, Florida (*5*). The presence of contaminants in eggs has been associated with the reported disrupted reproductive and developmental physiology of alligators (*6*). In fact, using an estrogen receptor assay from alligator, we showed that the individual chemicals had little or no activity (*7*). However, a combination of all the chemicals at concentrations found in the eggs produced synergistic binding activity with the alligator estrogen receptor.

By studying the activity of "naturally" occurring combinations, we can begin to understand the activity of chemical mixtures. In fact, because of the varied endocrine defects reported in the literature that

have been associated with environmental agents (6), it is likely that synergy in estrogen signaling and also in other endocrine systems is partly responsible for the reported effects.

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"Quantum Voodoo"

There is a very old method of communicating faster than the speed of light. You take a red marble and a green marble, and—without looking—place them in two different boxes. Your assistant takes one box and saunters off to the East Coast. You take your box and proceed to the West Coast. Then at a previously agreed upon time, you open your boxes. You will both "instantaneously" know what color marble your partner is looking at—even though you're thousands of miles apart! This experiment is even more impressive if you assume that until one of you actually looks at a marble, either one "could" be either color. (Try disproving that some time!)

I see now that quantum mechanicians are experimenting with making "the quantum state of a particle . . . disappear, then reappear elsewhere . . . without physically making the trip" (G. Taubes, Research News, 25 Oct., p. 504). These are, indeed, exciting times.

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Flights from Reason?

The quote (Random Samples, 11 Oct., p. 183) from Norman Levitt's book *The Flight from Science and Reason* (*1*) exhibits a flight from reason equivalent to that apparent in many postmodernistic critiques of "science." Specifically, "the idea that the cultural critic can meaningfully analyze . . . " anything or everything does not follow from the premise that "everything that people do is 'cultural.' " It may be "distinctly weird to listen to pronouncements on the nature of mathematics from the lips of someone who cannot tell you what a complex number is," but it does not follow that those pronouncements have no empirical validity. The explicit methods of study that constitute "science" were created to address the question of how we can establish empirical validity. This question arises only because all human understanding *is* "culture."

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