Letters

Synthetic Elicitors

We would like to draw attention to an error in Thomas H. Maugh II's article "Exploring plant resistance to insects" (Research News, 14 May, p. 722) pertaining to a description of our work on synthetic elicitors. He reports that both aryl cluster glycosides and fluorinated carbohydrates stimulate production of phytoalexins in soybeans about ten times as effectively as naturally occurring elicitors. This is incorrect; both series of compounds were determined to be inactive by the soybean cotyledon bioassay.

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Mycotoxin Weapons

In Eliot Marshall's article "The Soviet elephant grass theory" (News and Comment, 2 July, p. 32), Paul Nelson is quoted as saying that he "has never come across any reference to a toxin-producing *Fusarium* in Vietnam, Laos, or Kampuchea." In fact, no one has systematically surveyed the area for toxigenic fusaria. To our knowledge, the four trichothecene-positive samples collected from sites of "yellow rain" attacks were not examined for the presence of toxin-producing fungi.

In Marshall's article "Yellow rain: Filling in the gaps" (News and Comment, 2 July, p. 31), the value of T2 toxin as a weapon is questioned because of high cost: "Researchers must pay $7000 or more for a gram of the most potent variety of T2." This point confuses the issue. First, there is only one "variety" of T2 toxin. Second, the $7000 per gram price is extrapolated from 10-milligram analytical standards. Moreover, even the Department of State maintains that crude extracts are being used. It is our view that such crude extracts would be simple and inexpensive to produce and could be manufactured by Southeast Asian countries. The processes involved are described in the open scientific literature [for example, see (*1*)].

Readers of Marshall's articles might conclude that high toxin-producing strains of *Fusarium* are unavailable. In fact, highly toxic strains are available with virtually no security checks from dozens of laboratories and culture collections.

The evidence, to date, for Soviet complicity in the production of mycotoxin weapons rests on a listing (*2*) of Soviet scientists involved in mycotoxin research and the existence of fermentation facilities in the Soviet Union. Clearly, by this standard of circumstantial evidence, we must also be occupied with such diabolical pursuits. Why then is our government so eager to condemn our Soviet colleagues?

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References

1. H. R. Burmeister, *Appl. Microbiol.* **21**, 739 (1971).
2. *Report on Yellow Rain* (Department of State, Washington, D.C., 22 March 1982).

An unanswered question in the article by Eliot Marshall describing the use of mycotoxins in Kampuchea is why T2 toxin was present in blood samples from people 2 weeks or more after exposure. I suggest that this is best explained by a sequestering of the chemical in certain organs, particularly the kidney, rather than by binding to serum albumin, as was proposed. Many drugs have a high affinity for albumin, including, for example, clofibrate, warfarin, and most of the aspirin-like compounds; yet all of these are eliminated quite rapidly from the body (*1*). Other chemicals, such as gentamicin and ochratoxin A, have quite different binding affinities toward albumin; yet both are concentrated to a high degree in the proximal tubules of the kidney and are eliminated very slowly from the body over a period of time. Thus, the binding and accumulation of trichothecenes in the kidney, followed by a slow elimination phase, would account for the appearance of measurable quantities found in victims weeks after exposure.

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References

1. A. G. Gilman, L. Goodman, A. Gilman, *The Pharmacological Basis of Therapeutics* (Macmillan, New York, ed. 6, 1980).

The article by Eliot Marshall "Yellow rain: Filling in the gaps" is a fairly accurate account of the feelings of various U.S. *Fusarium* and trichothecene specialists concerning this topic. Most believe that, indeed, (i) *Fusarium* toxins have been found in Southeast Asia; (ii) they are not of natural origin; (iii) they could explain a majority of the signs and symptoms described, although reservation exists as to the rapidity of the onset of hemorrhaging; and (iv) T2 and HT2 have been found in blood and urine of victims, but it is difficult to understand why residue was found in victims 18 days after exposure.

Our laboratory has been involved in the analysis of various *Fusarium* toxins since 1963 and draws on this experience in coping with the analysis of trichothecenes in various substrates. Since 1970 we have developed and used a combination of gas chromatography and mass spectroscopy in the detection and quantitation of these mycotoxins. Our present mass spectral analytical approach includes selected ion monitoring in both the electron impact and positive chemical ionization mode. Our resolution is done on 15- and 30-meter capillary columns, so that retention times are very precise. In all selected ion monitoring analyses, we insist on a minimum of a base peak and a molecular ion with the correct ratio of intensity before a positive identification is made. When possible, we obtain a full mass spectral scan to support our conclusion. My assistant Robert Pawlosky (mass spectrometer operator) and I have a high degree of confidence in our results and hence take a positive view in the questions we ask, namely, What organs are involved in binding the T2 residue? Can T2 and metabolites in blood and urine be used as a diagnostic tool by a veterinary diagnostician? And what are the effects on metabolism of T2 when the liver and kidney are overwhelmed with a toxic dose?

I believe Marshall's article should have stressed more poignantly that T2

and HT2 were found in the blood and urine drawn from victims 24 hours after exposure. The concentrations were substantial and the identification unequivocal. Victims such as these are hard to come by, and the data obtained force one to a logical conclusion that these people were exposed to large doses of toxins impossible to obtain from natural contamination. The T2 residue obtained from victims exposed 18 days earlier is more difficult to explain from our present-day knowledge of T2 metabolism, although the analytical data are sound. We know that ochratoxin A has approximately a 3-day half-life in the blood of swine and that zearalenone has a half-life of 26 hours in bovine serum (data from our laboratory); perhaps it is not surprising that trace amounts of T2 and HT2 were found in humans 18 days after exposure. We do not know what residue to expect in a human system exposed to large doses of toxin that could realistically overwhelm the detoxification system of the liver. Experiments conducted in our laboratory showed that a cow intubated with a single dose of T2 toxin (180 milligrams) contained 8.4 parts per billion (ppb) T2 4 hours after exposure and 5.9, 1.1, and 0.5 ppb after 8, 16, and 20 hours, respectively. Moreover, metabolic studies of tritiated T2 toxin in a cow showed radioactivity in the plasma equivalent to 10.2 ppb 3 days after single-dose exposure. These results are in contradistinction to those reported by W. Buck and S. Swanson (*1*), where intravenous administration was used and no T2 could be found a few hours after treatment (half-life of 10 minutes). I am not certain that intravenous administration is meaningful in half-life calculations of T2 in humans where exposure is affected by inhalation and absorption through the skin and the contact time of toxin is not known. Moreover, our findings have shown that other metabolites, such as TC1, neosolaniol, HT2, TC3, 4-deacetylneosolaniol, TC6, and TC8 were found in bovine plasma 20 hours after exposure at concentrations of 3.8, 0.6, 0.3, 2.6, 0.8, 7.5, and 9.1 ppb, respectively. Collectively this represents a total of 25.4 ppb of trichothecene metabolites 20 hours after exposure. We can detect less than 1 ppb of T2 and HT2 toxins and feel that the low concentrations found are reasonable, particularly where the data on amount and duration of exposure of victims are lacking and the metabolism in humans is unknown. It would be unscientific to ignore the residue found by empirical means on the grounds of theoretical considerations.

One last comment on the cost of T2 production for large-scale use: If one were to prepare pure crystals of T2 or diacetoxyscirpenol, then the cost would be prohibitive. However, the preparations used are crude and contain a mixture of fungal metabolites. Crude culture extracts with a minimum of preparation would be cost-efficient.

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References

1. W. Buck and S. Swanson, paper presented at the meeting of NC129, North-Central Regional Mycotoxin Committee, U.S. Department of Agriculture, Denver, Colo., March 1982.

Correct Attributions

I would like to make two small corrections to the careful account by Jean L. Marx (Research News, 9 July, p. 141) of the recent work of Behan and myself on the associations of left-handedness.

The article attributes to me and Marian Diamond of Berkeley the discovery of sex-related anatomic differences in the brains of rats. In fact, the credit for this discovery is due only to Diamond and her co-workers. Following up her work, Albert Galaburda of my department confirmed by a different group of measurements the presence of asymmetry in the rat brain.

In addition, the article attributes in part to me the credit for discovering the abnormalities in the brain of a childhood dyslexic. This finding was the work of Galaburda and Thomas Kemper.

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Related Incidents?

It appears that the recent detention and expulsion of Lisa Wichser from the People's Republic of China was probably in retaliation for the initial diplomatic incident, when the luggage belonging to ten Chinese nationals, five of whom were diplomats, was searched in New York on 6 May (News and Comment, 11 June, p. 1204). It is a common occurence for countries to respond to one diplomatic offense with a similar incident; in this case there are several similarities between the two incidents. Both involved students on exchange programs and questions concerning information flow. Even the statements made by people involved in the incident are similar. For instance, the statement by Chinese official Li Jia Zhao, "As far as we know, everything was public information," sounds similar to Wichser's statement, "They weren't state secrets." In each case, these people were refering to documents being used and transported by the exchange students.

While the initial incident, the U.S. search of diplomatic luggage, was clearly in violation of international convention, the second incident, the Chinese search and detention, was legal but more serious because an expulsion resulted from it. The State Department should be aware that the latter incident may be intended to put the United States on notice that the Chinese will not stand for petty harassment, in which the Reagan Administration has been involved, of the nationals of socialist and communist nations.

Many scholars feel that the United States has as much to gain from exchanges as the People's Republic of China and the Soviet Union; while we need social science information predominantly, they need technical information. If we limit the access of unclassified technical information, these countries may increase restrictions on their social science and technical information. We cannot expect to get something for nothing.

It is interesting that the U.S. press generally did not mention the Chinese luggage incident with any degree of import (in some newspapers, the incident was not reported at all), while Wichser's expulsion was widely reported as a major incident. Moreover, the press usually gave the main reason for the incident as Wichser's engagement to a Chinese national. To my knowledge, the press has not attempted to connect the two incidents, even though they appear linked; nor has the press noted that the restrictions the People's Republic of China places on information flow to foreign nations are not altogether different from the restrictions the Reagan Administration is imposing.

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Erratum: The credit line for the cover photo of the 30 July issue should have included, in addition to Raymond T. Bartus, Reginald L. Dean and Marc S. Abel at the Lederle Laboratories, American Cyanamid Company, Pearl River, New York 10965.

Erratum: The sentence beginning on line 6 of the cover legend for the issue of 2 July should have read, "The stomach can be seen filled with ingested algae, and to the *right* of the stomach. . . ."