

Lederberg

DEPARTMENT OF BIOCHEMISTRY AND MOLECULAR BIOLOGY
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Joshua Lederberg, President
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Dear Josh,

Here are some items of interest in connection with the "yellow rain."

I think you would find it interesting to talk with Sorenson by telephone (304-599-7516). He administered T-2 solution to rats by tracheal instillation. At lethal doses he found massive lymphatic damage but little or no local damage in the lungs and no gross hemorrhage anywhere in the body. His interpretation is that the mycotoxin is transported out of the respiratory system too rapidly for detectable damage to have resulted. Of course the alveoli may respond differently and a solid aerosol may give different results, but these things remain to be demonstrated.

In certain forms of malnutrition, hemorrhaging from mucus membranes is not uncommon. Is it possible that the target populations include malnourished individuals with a resultant sensitivity to trichothecenes considerably greater than that expected on the basis of the existing literature?

As I testified at the Senate hearing last week, I think we have preliminary evidence for the use of mycotoxins. Nevertheless, considering the historic importance of the matters involved and the high value that must be placed on the credibility of the US government, I believe that the case is very seriously incomplete. One concern is the possible natural systemic occurrence of the toxins in certain higher plants. These materials are powerful insecticides and phytotoxins and may play important roles in the natural ecology of various regions. The feeling of some experts that systemic occurrence in higher plants is unlikely must be discounted because of the fact that, with one exception, all the species hitherto examined are crop plants. Species given to systemic accumulation of mycotoxins would not have been chosen by man as crop plants. The only non-crop plant that has been analyzed, so far as I know, does contain trichothecenes, 200-300 ppm of the macrocyclic baccharinoids. The trichothecenes seem to be derived from a soil fungus, absorbed through the roots and stored in the plant. Jarvis finds that this effectively protects the plant against certain leaf sucking

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insects. This biological perspective underscores what is obvious: we need analyses from the attack areas and from comparable unattacked sites nearby, both in reasonable numbers, and using plant material of the same species growing under similar conditions. There is only one plant sample analyzed from an attack area, so far as I know. Sharon Watson said last week that there are also two control samples of the same species. As I understand it, the positive sample weighed about 0.4 grams and consisted only of leaf and stem. Species identification, especially in the tropics, usually requires inspection of flowers and/or fruits. Without knowing just how the species identification was accomplished, I am skeptical of its accuracy.

I was puzzled by Richard Burt's statement last week that the person bringing back water containing 66 ppm deoxynivalenol became "gravely ill" after spilling some of it on himself. Vesonder at Peoria has come in contact with stronger solutions with no ill effect. Amongst the obvious possibilities, if the story is not a gross exaggeration, is that some as yet unidentified substance in the water was responsible.

In trying to think of chemical tests that would shed light on the origin of the trichothecenes, I have wondered what high resolution mass spectrometry could tell us. Two things might be looked into. First, carbon isotope ratios can be used to distinguish the major photosynthetic pathways used by higher plants. This might allow some deductions regarding the substrate on which the fungus grew. Second, hydrogen or oxygen isotope ratios might provide information regarding temperatures of synthesis.

Warm regards.

Sincerely yours,

Matthew Meselson

P.S. I also enclose the sanitized version of my review of the DSB CW Pand Report.

bcc: Dr. Robert Mikulak

- Enclosures:
- Burmeister, H. R. "T-2 Toxin Production by *Fusarium tricinatum* on Solid Substrate." *Applied Microbiology* 21:739-742, 1971.
 - Rukmini, C., Prasad, J. S. and Rao, K. "Effects of Feeding T-2 Toxin to Rats and Monkeys." *Food and Cosmetics Toxicology* 18:267-269, 1980.
 - Materials from AOAC Meeting, 21 October 1981.
 - Abstract of "Toxicity of Inhaled Mycotoxins," by W. Sorenson, from *Toxicology Research Projects Directory*, v.4, no.1, January 1979, page 1-43.
 - Jarvis, Bruce B., Midiwo, Jacob O. and Tuthill, David. "Interaction Between the Antibiotic Trichothecenes and the Higher Plant *Baccharis megapotamica*." *Science* 214:460-462, 1981.
 - Meselson, M. "Comments on the Defense Science Board (DSB) Chemical Warfare Panel Report." 8 January 1981.