

Yellow rain: Bee 'spring cleaning'?

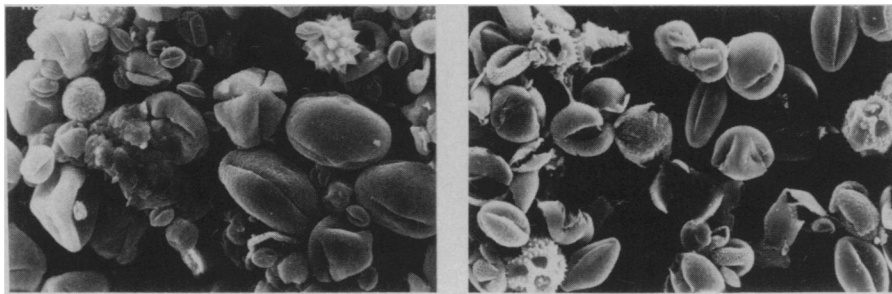
Bees of the genus *Apis* do not defecate in their hives, though they stay there all winter. But come spring, they take off on "cleansing flights," excreting the pollen that had been consumed in the nest. At the recent American Association for the Advancement of Science meeting in Detroit, biologist Matthew Meselson of Harvard University presented evidence that this bee-cleansing phenomenon may be the cause of the "yellow rain" spots in Southeast Asia that the U.S. government claims are the result of chemical warfare spraying. The U.S. State Department immediately dismissed the bee excrement theory, saying that the notion that yellow rain may be a natural phenomenon "has in fact been exhaustively studied, and subsequently rejected, by responsible and qualified scientists in and out of government."

For several years, the U.S. government has been amassing evidence to develop a case that proves Soviet-supplied poisons — based on toxins produced in nature by certain *Fusarium* fungi — are being used as chemical warfare agents in Southeast Asia (SN: 10/17/81, p. 250; 1/15/83, p. 40). The evidence ranges from eyewitness accounts of attacks to the finding of tricothecene mycotoxins (the poisons produced by *Fusarium* fungi) in samples of yellow rain and in the blood and urine of alleged attack victims. Such attacks would violate two international treaties: the 1925 Geneva Protocol and the 1972 Biological Weapons Convention.

Meselson — who counseled the White House, Defense Department, State Department and the Arms Control and Disarmament Agency on matters of chemical and biological warfare for 10 years, beginning under President John F. Kennedy's administration — has been one of the more vocal critics of the current administration's handling of its yellow rain case. He believes that the government has failed to scientifically address certain curious pieces of evidence: why, for example, are high levels of pollen present in the majority of yellow rain samples (some samples were not analyzed for pollen)?

Earlier this year, Meselson discussed the matter of yellow rain pollen with several colleagues, including Thomas D. Seeley of Yale University, an expert on the bees of Southeast Asia, and Peter S. Ashton of Harvard, an expert on Southeast Asian plants. The pieces of the puzzle — such as the reported size and spacing of yellow spots in affected areas — seemed to fit together neatly when the group took into account the spring-cleaning habits of the Southeast Asia *Apis* bees.

So in May, Meselson gathered from a leaf in Cambridge droppings from the spring-cleansing flights of bees related to those in Southeast Asia. With the aid of an electron



Electron microscope reveals that sample of yellow rain from an alleged attack (left) looks similar to bee excrement sample from Cambridge (right).

microscope, Meselson found that pollen grains from the Cambridge bee excrement resembled pollen grains found in yellow rain samples given to him by the Canadian government. He also found bee hairs and pollen grains similar to those in Cambridge bee excrement in a sample of yellow rain collected from Laos in 1981. On the basis of these findings, it is possible, Meselson and colleagues reported at the AAAS meeting, that yellow rain is little more than bee excrement.

The day following Meselson's report, the State Department issued a statement denouncing the bee theory, mostly on the grounds that it fails to take into account "the full range" of yellow rain evidence. The statement also contained an explanation of why it is unlikely bee droppings

could be the source of tricothecene mycotoxins, something that was never contended by Meselson in his report. Meselson reported that the bee droppings may be the source only of the yellow spots that have been discovered in Southeast Asia; the fungal toxins that have been found in the yellow rain spots, as well as in the blood and urine of alleged victims, could originate from naturally occurring *Fusarium* fungi, Meselson says.

But even if both the yellow spots and tricothecene mycotoxins have natural sources, Meselson says, "it doesn't mean that there isn't some form of chemical warfare going on in Southeast Asia and that we just haven't identified the correct agent yet." Says Meselson, "The subject needs to be looked at afresh." — L. Garmon

Anti-cancer drug disguise fools tumor cells

Tumor cells can be fooled. Recently, researchers demonstrated that anti-cancer drugs masquerading as blood clots can fool tumor cells into switching on the drugs, which then destroy the tumor cells. This finding was reported in the May JOURNAL OF MEDICINAL CHEMISTRY by Philip L. Carl of the University of North Carolina Medical School in Chapel Hill and colleagues Prasun K. Chakravarty, Michael J. Weber and John A. Katzenellenbogen of the University of Illinois in Urbana.

The researchers modified anti-cancer compounds, such as Adriamycin, which is widely used in chemotherapy, by binding them to proteins similar to those found in blood clots. When tested in animal cell cultures, the drugs were much more toxic to malignant cells — which activate the drugs by cleaving the protein — than they were to normal cells, suggesting that this modification makes the drugs more selective.

Carl chose to package the drug in this particular protein because tumors exhibit an increased level of plasmin, an enzyme that breaks down fibrin, a protein that forms the framework of blood clots. The drug appears to the tumor as a fibrin clot, and the increased amount of plasmin in the tumor area eats away the small protein, activating the drug. The drug, inactive when bound to the protein, then only kills cells in those areas of high plasmin activity — at the tumor site.

For most anti-cancer drugs, explains Carl, "the difference between the toxic dose and the effective dose is pitifully small." So while anti-cancer drugs kill tumor cells, they also kill normal cells. By taking advantage of the biochemical differences between normal and malignant cells, Carl notes, "we don't necessarily make the drugs more effective for fighting cancer, just less toxic to normal cells."

Although the modified drugs were less toxic to normal cells in cell cultures, the researchers have yet to see any decreased toxicity in animal studies. "I must admit," Carl says, "we've been rather more successful with plastic dishes than we've been with animals." The biggest problem, Carl believes, is that in the intact animal other enzymes cleave the protein before the drug reaches the tumor site. Most hazardous to the protein is the trypsin it encounters in the stomach following absorption through the bloodstream. The activated drug is then reabsorbed out of the small intestine and circulated through the body. "Obviously, when this happens, you've lost the targeting," says Carl.

Now the researchers are seeking a drug that, if activated elsewhere, will not circulate to normal cells. Carl is looking into a drug called bleomycin, which is used to fight lung cancer. He observes that this drug does not appear to be reabsorbed. The next step, Carl says, is to test it in animals and see if that is true. — P. Taulbee