The Destroying Angel: A Story of a Search for an Antidote

Every year, from early spring until the time of the first frost, the destroying angel can be found throughout this land. It inhabits the woods, growing sometimes in clusters, sometimes in more solitary splendor. It grows in fields and pastures and even lawns, especially in places where trees have been recently cut down. It is particularly suited to ground that is low and wet.

Every year, some unwary mushroom fanciers partake of the destroying angel which has been described as an "exceedingly poisonous, dangerous, seductive species." Every year, many people die. No one knows how many—perhaps a dozen, perhaps more. There are no requirements for reporting wild mushroom poisonings; many cases may never be correctly diagnosed. As little as a teaspoon of the graceful destroying angel, *Amanita phalloides*, is enough to cause a painful, lingering death.

The destroying angel is an insidious killer. Most poisonous mushrooms make their presence quickly known, attacking the victim's gastrointestinal tract and causing nausea and vomiting shortly after being consumed. Not so the destroying angel. Its victims remain symptomless for hours, sometimes for as long as a full day, before they are seized by severe abdominal cramps, diarrhea, and vomiting. The mushroom toxins attack the liver, causing it to atrophy and fail. Eventually the patient becomes disoriented, goes into a hepatic (liver) coma, and dies. Death may not come for a week or more.

There is no certain antidote to *Amanita phalloides* poisoning, but there is some evidence that an Italian-made drug, thioctic acid, gives the dying victim a fighting chance.

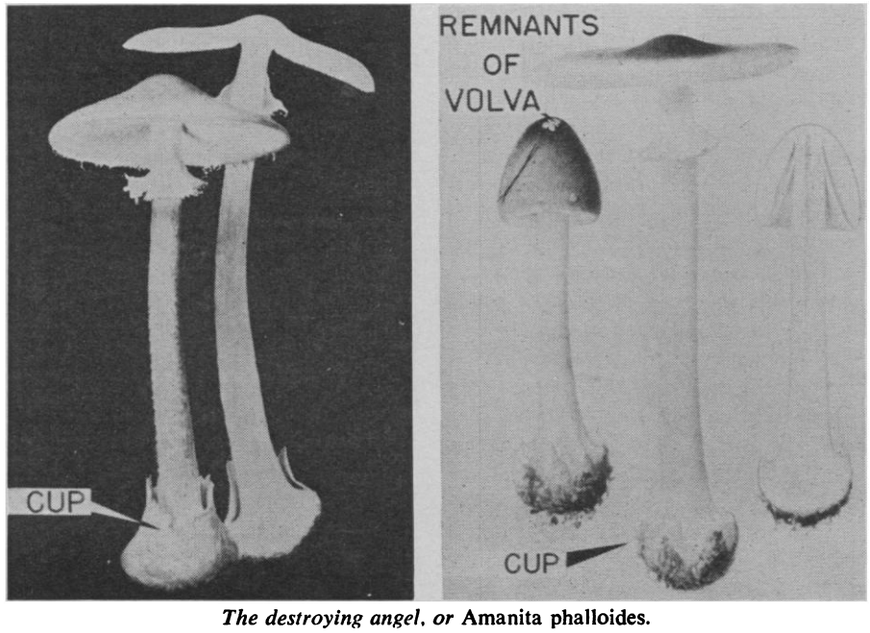
Most of the evidence of the drug's effectiveness comes from Europe. For more than a decade, investigators in Czechoslovakia have been using thioctic acid experimentally and have consistently reported considerable success in rescuing their poisoned patients from the throes of death. In one study, 39 of 40 persons poisoned by the destroying angel were saved. In Italy thioctic acid has reportedly been considered the therapy of choice since 1968.

The history of thioctic acid use in the United States is briefer. It is thought that it was first used in 1970 by a Temple University team who had it flown over from Naples where it is manufactured by Richardson-Merrell Spa, a division of Richardson-Merrell Inc. of New York. In that case, thioctic acid reportedly saved the life of a New Jersey man who, mushroom hunting in a pine grove, had unwittingly picked some *Amanita* that his wife used in a stew. Two persons died.

Now, for the first time, a channel for the distribution of thioctic acid in the United States has been established. The Food and Drug Administration (FDA) has granted an investigational new drug (IND) application to Frederic C. Bartter, clinical director of the National Heart and Lung Institute at the National Institutes of Health (NIH) in Bethesda, Maryland. Any physician with a patient poisoned by the destroying angel can call the NIH Clinical Center at any hour of the day or night to request the experimental drug. It will be flown out on the next plane, and Bartter or one of his colleagues will advise the physician about the drug's use. (A course of therapy should run about 2 weeks.) Eventually, researchers hope to accumulate enough data to know whether thioctic acid, which is considered to be somewhat controversial in this country, really is lifesaving.

Bartter, an endocrinologist, acquired the only thioctic acid IND in the United States somewhat by chance. It was not he who asked the FDA for it but the FDA that asked him to accept it: It seems that Richardson-Merrell did not want to make the heavy investment necessary to get thioctic acid through the various stages FDA requires before allowing a drug on the market. There simply is not enough demand to make it profitable. And FDA itself could not assume responsibility for the drug, even though on a couple of occasions in the last 2 or 3 years it has given it to physicians with dying patients. So, FDA officials, after learning that Bartter is a knowledgeable mycologist, asked him to help out. Bartter agreed.

Everything seemed to be in order last spring, and Bartter was preparing to notify hospitals across the country of the availability of the experimental antidote when some FDA toxicologists who had been testing thioctic acid in mice and dogs came up with data suggesting that it might actually cause more harm than good. Alan K. Done and his colleagues gave the animals very large doses of *Amanita* toxins and thioctic acid simultaneously. They appeared to be getting no protection from the toxins. In fact, it seemed that more



The destroying angel, or Amanita phalloides.

were dying sooner than if they had been left alone.

Bartter canceled plans to let physicians know about the IND. By then, it was early June. *Amanita* season had begun. Bartter and the FDA scientists conferred fairly frequently for a while, trying to reconcile the new animal data with clinical reports from abroad and from limited experience in the United States. According to Bartter, in this country thioctic acid has been tried in cases of *Amanita* poisoning only a handful of times. In four of five cases that were recorded in FDA's files, the victims had been cured. Both he and the FDA scientists were reluctant to abandon the IND and were reluctant to go ahead. The people at FDA conducted more experiments.

It was entirely possible, everyone agreed, that the animals were dying from severe glucose imbalance—low blood sugar. The mushroom toxins attack the liver; that, presumably, is where thioctic acid acts, too. "Anything that knocks out liver lowers blood sugar," Bartter says. "So, in the later experiments we carefully maintained glucose levels in the dogs, just as you routinely would in a patient. You'd never let a patient's blood sugar go down the way it did in those animals in the first experiment."

It appears that this was the problem. When dogs receiving toxin and antidote were also given glucose, they survived. The researchers decided then that it is reasonable to use thioctic acid experimentally to try to save the lives of victims of the destroying angel.

Thus far, Bartter has had one request for thioctic acid, from a physician in San Francisco whose patient was a young boy who was already in a hepatic coma when the call for the antidote came in. As the drug was being flown to California, the boy died. Bartter hopes that, next time, the call will come sooner.

—BARBARA J. CULLITON

Briefing

Senate Disputes Ruling on Double Bottom Tankers

Despite Administration promises to Congress, the U.S. Coast Guard has omitted the controversial double bottom safety feature from its currently proposed regulations for U.S. oil tankers. Legislation is now pending in the Senate that would override the Coast Guard's decision. Advocates of the double bottom tanker believe the omission compromises protection of the marine environment. The Coast Guard claims that imposing the standard would be a financial burden to the U.S. tanker fleet and would reduce total oil spillage only marginally.

The seeds of the controversy were sown when Congress was considering the Trans-Alaskan pipeline in 1972. Secretary of the Interior Rogers C. B. Morton, as the official government spokesman, stated that American tankers carrying oil from Valdez to other U.S. ports would be required to have double bottoms. The Coast Guard could have objected to the double bottom feature then or at any time since, but failed to do so, an Interior official told *Science*. Morton has not changed his position.

Opponents of the double bottom say it would raise construction costs by 10 percent. Nor would it help prevent oil spills: if the space between the two bottoms flooded with water in the case of a grounding, the stranded tanker would settle deeper and be harder to salvage. A UN-sponsored conference on marine pollution in 1973 rejected the double bottom as an international standard on these very grounds. Most oil companies oppose the double bottom for the same reasons, preferring less costly methods of oil spill prevention.

The Coast Guard abandoned its 2-year support of the double bottom on 28 June, offering no new technical information, but citing the fact that U.S. tankers with double bottoms would have higher cargo rates than their single bottom foreign competitors. Another reason was a desire to keep Coast Guard regulations consistent with international standards.

Neither reason has convinced double bottom supporters, and the Senate may require new U.S. tankers to have double bottoms after all. The Commerce Committee amended the House-passed Oil Cargo Preference bill to require this safety feature. Convinced earlier by the Coast Guard of the environmental value of the double bottom, Senators Warren Magnuson (D–Wash.), Edmund Muskie (D–Maine), and others appear unwilling to settle for anything less. The amended bill is expected to soon pass in the Senate.—D.S.K.

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Manufacture of Aldrin Is Suspended by EPA

Further manufacture of all pesticide products containing aldrin or its metabolite dieldrin has been suspended by the Environmental Protection Agency (EPA) as an "imminent hazard to the public." In his suspension order of 2 August, EPA Administrator Russell E. Train concluded, on the basis of studies conducted with test animals, that "the present estimated average human dietary intake of dieldrin subjects the human population to an extremely high cancer risk."

The order represents the first time that EPA has stopped the manufacture of a major insecticide upon an imminent-hazard determination and without awaiting the completion of hearings on petitions to ban the chemical permanently. Hearings on a petition by the Environmental Defense Fund (EDF) to ban aldrin have been under way since last summer but will not be completed for several more months. Without the suspension order, the Shell Chemical Company, manufacturer of aldrin, would begin this September to produce another 10 million pounds or more of the chemical for sale during the 1975 farming season (aldrin is used principally in the growing of corn). Shell has the right to demand an early hearing on the suspension, but its chances of having the order reversed appear remote.

The manufacture of aldrin was not suspended earlier because evidence of an imminent hazard had not been found convincing. But Train has concluded that the evidence presented this year by EPA's Office of Hazardous Materials Control is compelling.

"To await the 20 to 30 years of exposure [to dieldrin] necessary to determine the ultimate effect is only to wait until the damage to an entire generation of humans is complete," Train said. "We reject the 'body count' approach to protection against cancer or other long-term threats to public health."

—L.J.C.