Blighted Bounty: A Twist in the Staff of Life

Molds that produce carcinogenic toxins grow on many of the world's staple food crops

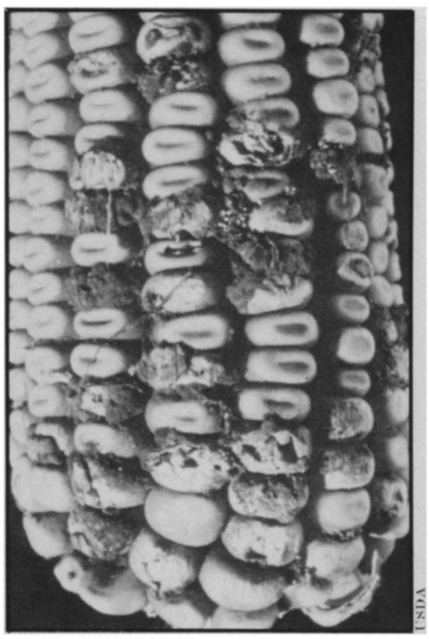
By Janet H. Weinberg

A scientific field was born in 1961 when thousands of British turkeys died. What started as the search for the cause of "turkey x disease" has grown into a large research effort aimed at controlling carcinogenic toxins that occur naturally in staple food crops all over the world. These toxins add a complicating factor to the growing problem of world hunger and pose a threat to human health. Research is now under way that may someday eliminate these unwanted contaminants.

After the outbreak of "turkey x disease" in England, scientists isolated a potent toxin from the turkeys' feed and pronounced it responsible for the fatal liver damage the animals suffered. The toxin was associated in the blighted peanut meal with the common mold *Aspergillus flavus*, and they named it "aflatoxin." Scientists began looking for toxins in feeds and grains infected by *A. flavus* and other mold species. They found a sinister collection of them. More than 100 mold species that produce toxins have been found growing on (and contaminating) peanuts, corn, rice, cottonseed meal, oats, hay, barley, sorghum, cassava, millet and other staple foods.

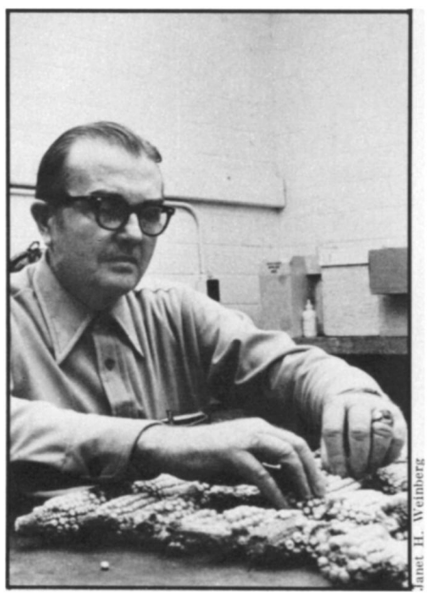
While some researchers in the new field looked for mycotoxins (the name for toxins from fungi) others looked at them. The emerging picture has been dark indeed. The toxins are formed when fungi invade whole or broken seeds and begin to consume the stored nutrients. Under certain temperature and moisture conditions, metabolic products are formed that are highly toxic to animals that consume the moldy foods. The toxins are harmful on two levels: The ingestion of high concentrations (several parts per million parts of the substrate, depending on the mold and type of food) can cause rapid degeneration of the liver; subacute concentrations (often just a few parts per billion parts of food) ingested over long periods of time can cause liver cancers to form.

A study just completed by biochemist G. N. Wogan of the Massachusetts Institute of Technology shows that about 10 percent of carcinogen-sensitive rats developed liver cancers after being fed just one part per billion of aflatoxin B_1 (the most commonly occurring mycotoxin) for 74 weeks. About 20 percent developed liver cancers when fed 15 parts per billion, 80 percent when fed 50 parts per billion and 100 percent died of cancer when fed 100 parts per billion. This establishes aflatoxin B_1 as one of the most potent carcinogens known.



USDA

Aflatoxin-producing mold on feed corn.



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Zuber: Screening corn varieties for natural resistance to molds and toxins.

It is difficult to generalize about the physical characteristics of mycotoxins. There are dozens of different chemical structures, many totally unrelated. The aflatoxins alone form a large class of highly oxygenated, heterocyclic compounds. Many species of *Penicillium*, *Fusarium* and other fungi genera also form variously structured toxins. Because they are so diverse, and the structures of some are still being described, there is no one biochemical theory of how the molecules act upon living systems. Wogan and others are currently studying the mode of action of aflatoxin B_1.

"We know that the toxin undergoes metabolic transformations in an animal's system, but where in the cells the ultimate metabolic form of the compound exerts its carcinogenic action is still unknown," Wogen says. It is thought that toxins are epoxidized after ingestion, and that the epoxide might be responsible for the carcinogenesis. "There is evidence that the toxin might bind to nucleic acids and cause an alteration in transcription of genetic information, but whether this has to do with the carcinogenic behavior is still unknown," Wogen says.

U.S. Food and Drug Administration and Department of Agriculture scientists began studying mycotoxins after early surveys showed a significant incidence of them in products in the United States. (These high levels have since been reduced.) The FDA is responsible for regulating the adulteration and contamination of foods, and mycotoxins are included in these categories.

Because the field was so new when

it became apparent that FDA surveillance for mycotoxins would be necessary, agency and agency-funded researchers in several research areas had to develop analytical methods for detecting toxins and do much of the basic descriptive work. They found out that mycotoxins are a messy and difficult subject to study.

Mycotoxins, it seems, can grow on stored foods, newly harvested foods and on foods still in the fields. Seeing molds does not necessarily mean that toxins are present, but seeing no evidence of mold growth does not mean they aren't, either. Tiny amounts of mold can grow in nearly invisible cracks in seed coats and produce toxins, and although many toxins fluoresce under ultraviolet light, chemical analysis is needed for ultimate identification. Mycotoxin contamination is often irregular and localized; outbreaks and incidence of toxins vary from year to year, commodity to commodity and county to county. Contamination can even occur in just one part of a truckload of corn, making routine sampling less than accurate. Toxin molecules are often so stable that they can survive food processing operations and can be passed on to meat, milk and eggs after an animal consumes them.

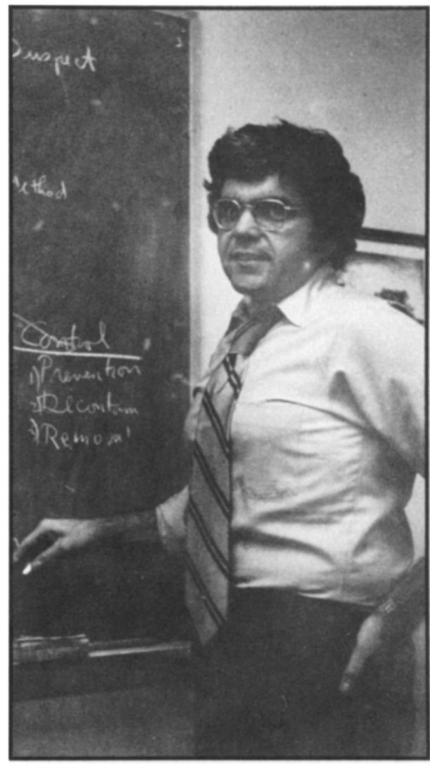
The task of coordinating and directing the complicated research effort has fallen largely to FDA scientist-administrator Joseph V. Rodricks. His FDA mycotoxin unit recently completed a proposal for the first official tolerance level for aflatoxins in peanut products sold for human consumption. Rodricks shared the hot-seat with FDA Administrator Alexander M. Schmidt when the tolerance level was announced in early December. The levels were dropped from 20 parts per billion to 15 parts per billion, but critics charge the drop was insubstantial, that allowing any toxic residues is unconscionable and that the new levels are designed so that few peanut processors will have to alter their current processing techniques and standards.

Schmidt says a zero tolerance level is probably not attainable and setting such a level might endanger U.S. food supplies. If weather conditions are conducive to toxin formation and large portions of crops are contaminated, a zero tolerance level would necessitate the destruction of needed food. "I will not have the agency locked into a situation which might ensure serious crop shortages," Schmidt says.

Because the occurrence of mycotoxins is so localized and variable, it is difficult to judge the economic impact. Clifford W. Hesseltine, a microbiologist at the USDA's research laboratory in Peoria, Ill., told SCIENCE NEWS that two to three percent of the corn crop might be lost each year through mold damage. Because it is difficult to remove all of the infected kernels from a partially contaminated lot, toxins inevitably will appear in animal feeds.

"The real problem here as I see it," Hesseltine says, "is that molds and toxins in feed result in decreased animal growth." He and four other agricultural reseachers did a study in 1971 which showed that various *Aspergillus* toxins can decrease normal growth rates in chicks and mice from 2 to 15 percent. The total loss to meat, milk and egg production from decreased growth rates is incalculable, but Hesseltine thinks the broiler chicken production, for example, could be decreased by as much as four percent per year.

Toxin contamination of feed corn has increased since the advent of the picker-sheller, a farm machine that



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Rodricks: Monitoring mycotoxin levels.

picks the ears when they still contain about 25 percent moisture, and strips the kernels from each ear. This often breaks the kernels and exposes them to fungal infection. Hesseltine calls the increase a "trade-off between technology and loss of yield. In order to harvest the bigger and bigger crops, we need technology, but we have developed picking and storing techniques without too much regard for mold growth."

Advanced transportation and storage systems, dry northern climates and the watchful eyes of the FDA and USDA probaby make up for the increased susceptibility due to mechanized farming, though, and toxin residues in food in the United States are minimal compared with foods in other parts of the world. Surveys of peanuts, cassava, rice and other human staple foods in Africa, India and Southeast Asia routinely have shown high toxin levels. In South Africa, for example, a 1971 survey of peanuts, corn, rice and manioc detected more than 1,000 parts per billion of aflatoxin B_1 in the foods.

The contaminated foods in these countries are taking their toll of human lives. FDA chemist Leonard Stoloff and biochemist T. Colin Campbell of Virginia Polytechnic Institute in Blacksburg reviewed the impact of mycotoxins on human health in the November JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY. Lacking direct experimental proof that mycotoxin consumption can cause human liver cancer, scientists have shied away from making such statements. But epidemiological data have now accumulated to such a degree that the conclusion is unavoidable. Campbell and Stoloff cite studies done in Thailand, Swaziland and other developing countries that show a positive correlation between the regular ingestion of foods containing high mycotoxin levels and higher than normal incidence of liver disease and cancer.

Stoloff studied cancer data from four areas of the United States but found no evidence of a correlation between liver cancer rates and mycotoxin ingestion.

In most societies, moldy foods are fed to livestock or discarded. But, says Rodricks, "If the alternative is starvation or famine, the destruction of food, even contaminated food, becomes a serious moral question." Control of toxin contamination is therefore a desirable objective, and several USDA scientists are currently researching possible control methods.

Hesseltine, Alfred C. Beckwith and others at the USDA's Peoria station have developed an experimental system for detoxifying whole corn contaminated with aflatoxin B_1. There are several chemical agents that can reduce aflatoxin levels in foodstuffs, but most of them either fail to destroy some types of toxins or decrease the nutritive value of the commodity. Beckwith reported to the American Chemical Society in August the successful use of ammonia gas at elevated temperatures and pressures to detoxify corn. Ammoniation has also been tried on peanut and cottonseed meal with encouraging results. Ammoniation can reduce toxin levels by 95 to 98 percent, and the breakdown products of the toxins and ammonia do not seem to harm test animals. Engineers at the Peoria station are working on ways to apply ammonia to corn while it is stored in large bins.

Hesseltine says preventing mold development by using enlightened agricultural practices is an important and

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more immediate control measure. Since high moisture levels induce mold growth, the harvesting of drier corn and the better digging and drying of peanuts can help prevent contamination. Corn often is dried mechanically, and small dryer capacity, large harvests and scarce fuel supplies often prevent corn from being dried before it can mold in storage. Leaks in storage bins often re-wet commodities and should be repaired. High-moisture corn varieties can be blended with drier varieties and if done properly, can retard mold growth. The buildup of carbon dioxide during storage can prevent toxin formation, and many feed-lot owners are switching to bins designed for carbon-dioxide buildup.

These prevention measures, though, are applicable mainly to mechanized, technologically advanced agricultural systems and not to the systems of developing nations. "My personal feeling," Hesseltine says, "is that in the long run, the most promising approach to control of mycotoxins is the development of crops with genetic resistance to mold growth and toxin production."

One investigator working on this problem is corn geneticist Marcus S. Zuber of USDA's Agricultural Research Service and the University of Missouri at Columbia. Zuber is screening hybrid corn lines adapted to the cornbelt and "exotic strains" from Central and South America and Africa, hoping to find varieties with natural resistance to mold growth. He is also studying the link between insect damage and mold growth, since fungal spores have to be carried into the kernels through a break or tear in the kernel's outer covering. Kernels with thicker coverings may be more resistant to breaks and tears, Zuber says, so he is testing thick and thin "skinned" corn varieties.

An interesting sideline to the corn research, Zuber says, is the search for a natural toxin inhibitor. It is known that *Aspergillus flavus* will grow on soybeans, but no aflatoxin is formed on that substrate. "The big question is why, and all we have right now are wild guesses. We know that soybeans are high in trypsin inhibitor, but we don't know if this is important." If an inhibitor gene can be found and bred into the genetic complement of corn and other commodities, toxin formation could someday be prevented, regardless of harvesting, storage and processing techniques. This solution would therefore, be the most practical one for developing nations.

The study of mycotoxins, born in 1961, has already amassed an extensive body of information. Complete control of the unwanted contaminants, however, lies years away. □

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er of sediments east of Cape Hatteras that was unexpectedly rich in metals, well mixed into the other sediments. Usually, says Ewing, such metallic deposits are concentrated near the sediment-hard-rock boundary. How did they get mixed in? Answering such questions is likely to require going back to the source—which is just what IPOD is doing.

Drilling into more than a mile of hard rock beneath thousands of yards of sediment and water is an ambitious undertaking. When IPOD gets under way next fall, the Challenger team may find itself spending more than two months at a single hole. The ship may well have to pull up its drill string occasionally, return to port for restocking and go back to the hole again. Fortunately, the project has already developed and successfully applied a technique for relocating and reentering a hole. A more difficult task will be to find improved methods of recording the magnetic orientation of the core samples—which way was north when the core was in the ground? Patterns of magnetism in the rocks are clues to their ages, as well as to the heating and cooling to which they have been subjected. In addition, says Melvin Peterson of Scripps, careful surveying of proposed sites, more accurate positioning of the ship and increased reliability of the drill system will be needed.

Beyond the hard-rock drilling, perhaps four years away, the project's planners hope to tackle an even more ambitious objective: probing the vast accumulations of sediments—possibly more than three miles thick—that lie along the margins of the continents. These continental sediments should preserve detailed records of changing climate and evolving life forms going back to even before the great land masses rose above the waves.

So IPOD is not really changing directions; it is broadening its focus. Seismic velocity spectra, magnetic signatures and other such data are merely tools, not even the answers to the real questions. IPOD, in fact, may well reveal whole new questions to be asked. The first IPOD holes are likely to begin next September in the North Atlantic, probably in the vicinity of the Mid-Atlantic Rift. The Deep Sea Drilling Project sprang from redirection of Project Mohole, a plan to drill into the Mohorovicic Discontinuity between the earth's crust and mantle. IPOD will not get that deep, but it is asking—and answering—some of the same questions. □