PERSPECTIVE

Time to face the fungal threat

Changing crop selection and improving food storage might reduce global rates of liver cancer, says **Felicia Wu**.

Moulds that grow naturally on food can produce toxins that have serious effects on health, even causing cancer. Certain moulds — especially those that grow in maize (corn), peanuts and tree nuts such as almonds and pistachios — produce aflatoxin, a carcinogen that is estimated to cause up to 28% of the total worldwide cases of hepatocellular carcinoma (HCC), the most common form of liver cancer^{1,2}. Many people are unaware of the link between naturally occurring food contaminants and cancer. Education, stricter food-quality controls and the cultivation of alternative crops can have a large impact on worldwide rates of liver cancer.

Aflatoxin is generated by the fungi *Aspergillus flavus* and *Aspergillus parasiticus* and, in addition to liver cancer, it has been associated with acute poisoning, immune-system dysfunction and stunted growth in children. People whose livers are already compromised by infection with hepatitis B virus (HBV) are particularly susceptible to aflatoxin-induced liver cancer³.

Studies by my team^{1,2} suggest that up to 172,000 cases of HCC per year can be attributed to exposure to aflatoxin in the diet, and most of these individuals are infected with HBV. The majority of cases occur in sub-Saharan Africa, southeast Asia and the western Pacific region (including China), as well as in parts of Central America.

TOXIN CONTROL

Although around 100 nations have set standards for the maximum amount of aflatoxin allowable in foodstuffs, setting a standard does not always ensure a safe food supply — particularly among subsistence farmers and rural communities in low-income countries, where food rarely undergoes formal safety inspection. Unfortunately, these countries also often have the highest levels of aflatoxin in their crops. And adding to the complexity is the fact that different nations consume different amounts of the riskiest crops. The United States and Kenya, for example, both have maximum allowable aflatoxin levels of 20 micrograms per kilogram of maize, but the average Kenyan consumes six times more maize per day than the average American, and usually in a less-processed form.

Aflatoxin-induced liver cancer can be prevented, but doing so will take a coordinated effort. One part of the solution is widespread vaccination against HBV, which would rob the toxin of its partner in carcinogenicity⁴ (see page S12). Beyond immunization, decreasing contamination can be implemented with little cost to farmers. Stressed plants are more vulnerable to fungal infection, so the best prevention is a healthy field of crops. This can be fostered in numerous ways, including the careful selection of crop varieties that are matched to the soil and water conditions, improved irrigation practices to reduce drought stress, and by breeding crops for both high yield and the ability to withstand environmental stressors, such as heat, drought and insect damage. Beyond stress prevention, farmers can use fungi that do not produce aflatoxin to compete with the *Aspergillus* species and prevent them from colonizing crops⁵.

Growing the food is just part of the problem, however: aflatoxin also accumulates in crops after they have been harvested. The fungi that produce aflatoxins thrive in damp conditions, so storage facilities must be kept cool and dry. Pests such as rodents and insects must be controlled because they can transport the fungus to other stored foods⁶. If these tactics fail and the food gets contaminated, it can still be salvaged: clays or chlorophyllin (chlorophyll-derived compounds) can be added to the food, either before or after distribution to consumers, to temporarily sequester aflatoxin in the gastrointestinal tract^{7,8}.

The simplest solution is to reduce consumption of foods that are contaminated with aflatoxin. Dietary changes in Qidong, China, show just how effective this can be. Market reforms introduced in the 1980s meant that citizens in the area began eating more rice and less maize. Decreased maize consumption (from around 100 kilograms per person in the 1970s to almost none in 2012) resulted in lower exposure to

aflatoxin in the diet and a 45% decrease in liver-cancer mortality⁹. This effect is independent of China's HBV vaccination programme, which began in 2002.

Qidong provides evidence that introducing dietary diversity can reduce the effects of aflatoxin-related liver cancer. But diverse diets serve another purpose: the various essential amino acids and other compounds found in leafy green, cruciferous and *Allium* vegetables can help to nullify dietary toxins¹⁰.

Now, it is crucial to disseminate these interventions and encourage those populations at the highest risk to adopt them. Locally, educators must encourage communities to grow and consume foods that are less likely to be infected with *Aspergillus*. But because dietary change occurs slowly, they should also help communities to

choose geographically suitable maize and peanut varieties and teach them practices that minimize post-harvest aflatoxin accumulation.

Globally, the HBV vaccine must be disseminated to high-risk populations at increased risk of aflatoxin exposure. And as the prevalence of hepatitis C virus (HCV) increases worldwide, researchers must investigate the potential synergism of HCV and aflatoxin exposure. Only then will rates of these preventable cases of liver cancer begin to decline. ■

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