



February 2018

REF. No.: WHO/NHM/FOS/RAM/18.1

Department of Food Safety and Zoonoses

Aflatoxins

Aflatoxins pose a serious health risk to humans and livestock

Aflatoxins are poisonous substances produced by certain kinds of fungi (moulds) that are found naturally all over the world; they can contaminate food crops and pose a serious health threat to humans and livestock.

Aflatoxins also pose a significant economic burden, causing an estimated 25% or more of the world's food crops to be destroyed annually.

Most human exposure comes from nuts and grains

Two closely related species of fungi are mainly responsible for producing the aflatoxins of public health significance: *Aspergillus flavus* and *A. parasiticus*. Under favourable conditions typically found in tropical and subtropical regions, including high temperatures and high humidity, these moulds, normally found on dead and decaying vegetation, can invade food crops.

Drought stress, insect damage and poor storage can also contribute to higher occurrence of the moulds including in more temperate regions.

Several types of aflatoxin (14 or more) occur in nature, but four – aflatoxins B₁, B₂, G₁ and G₂ are particularly dangerous to humans and animals as they have been found in all major food crops; but most human exposure comes from contaminated nuts, grains and their derived products. Additionally, aflatoxin M₁ (AFM₁), a product of aflatoxin B₁ (AFB₁) metabolism, can be found in milk in areas of high aflatoxin exposure. Subsequently humans may be exposed to this aflatoxin through milk and milk products, including breast milk, especially in areas where the poorest quality grain is used for animal feed.

Food crops can become contaminated both before and after harvesting. Pre-harvest contamination with aflatoxins is mainly limited to maize, cottonseed, peanuts and tree nuts. Post-harvest contamination can be found in a variety of other crops such as coffee, rice and spices. Improper storage under conditions that favour mould growth (warm and humid storage environments) can typically lead to levels of contamination much higher than those found in the field.

Dietary exposure can vary greatly

National estimates of dietary exposure to aflatoxins indicate differences between developed and developing countries. In developed countries, mean aflatoxin dietary exposures are generally less than 1 ng/kg body

weight (bw) per day (a nanogram is one billionth [1×10^{-9}] of a gram), whereas estimates for some sub-Saharan African countries exceed 100 ng/kg bw per day, although these latter estimates are often based on very few data. Estimates of dietary exposure to AFM1 have rarely exceeded 1 ng/kg bw per day in any country (although up to 6.5 and 8.8 ng/kg bw per day for young children and breastfed infants have been reported).

Long-term exposure can have serious health consequences

Long-term or chronic exposure to aflatoxins has several health consequences including:

- ◆ aflatoxins are potent carcinogens and may affect all organ systems, especially the liver and kidneys; they cause liver cancer, and have been linked to other types of cancer – AFB₁ is known to be carcinogenic in humans; the potency of aflatoxin to cause liver cancer is significantly enhanced in the presence of infection with hepatitis B virus (HBV);
- ◆ aflatoxins are mutagenic in bacteria (affect the DNA), genotoxic, and have the potential to cause birth defects in children;
- ◆ children may become stunted, although these data have yet to be confirmed because other factors also contribute to growth faltering e.g. low socioeconomic status, chronic diarrhoea, infectious diseases, malnutrition;
- ◆ aflatoxins cause immunosuppression, therefore may decrease resistance to infectious agents (e.g. HIV, tuberculosis);



Aflatoxin contaminated nuts

Acute poisoning can be life threatening

Large doses of aflatoxins lead to acute poisoning (aflatoxicosis) that can be life threatening, usually through damage to the liver. Outbreaks of acute liver failure (jaundice, lethargy, nausea, death), identified as aflatoxicosis, have been observed in human populations since the 1960s. Most recently deaths attributed to aflatoxins were reported during the summer of 2016 in the United Republic of Tanzania. Adults are more tolerant to acute exposure than children. The consumption of food containing aflatoxin concentrations of 1 mg/kg or higher has been suspected to cause aflatoxicosis. Based on past outbreaks it has been estimated that, when consumed over a period of 1–3 weeks, an AFB₁ dose of 20–120 μ g/kg bw per day (μ gram is one billionth [1×10^{-9}] of a kilogram) is acutely toxic and potentially lethal.

In animals, aflatoxins cause a variety of adverse effects

In chickens, the effects of aflatoxins include liver damage, impaired productivity and reproductive efficiency, decreased egg production, inferior eggshell quality, inferior carcass quality and increased susceptibility to disease. Pigs are also highly affected by aflatoxins, with the chronic effects largely apparent as liver damage. In cattle, the primary symptoms are reduced weight gain as well as liver and kidney damage; where milk production is also reduced. Different forms of the enzymes that metabolize aflatoxins (e.g. cytochrome P450s, glutathione S-transferases) are considered responsible for the different susceptibilities of different animals to the toxic effects of aflatoxins.

Detecting aflatoxicosis in humans and animals is difficult

Detecting aflatoxicosis in humans and animals is difficult due to variations in clinical signs and the presence of other factors such as suppression of the immune system caused by an infectious disease. Of the two techniques most often used to detect levels of aflatoxins in humans, one measures a breakdown product in urine (which however is only present for 24 hours after exposure), and the other measures the level of

an AFB–albumin compound in the blood serum, providing information on exposure over weeks or months. These biomarker measurements are important in investigating outbreaks where aflatoxin contamination is suspected.

A variety of methods to detect aflatoxins in food and feed are available for different needs

Aflatoxins are of major importance and techniques for their detection and analysis have been extensively researched to develop those that are highly specific, useful and practical. A plethora of methods are available for different needs, ranging from techniques/methods for regulatory control in official laboratories (such as HPLC-MS [high-performance liquid chromatography-mass spectrometry]) to rapid test kits for factories and grain silos (such as ELISA [enzyme-linked immunosorbent assay]). Potential novel aflatoxin-detection systems, based on emerging technologies, include dip-stick kits, hyperspectral imaging, electronic noses, molecularly imprinted polymers, and aptamer-based biosensors (small organic molecules that can bind specific target molecules). The latter technologies may have relevance in remote areas because of their stability, ease of production and use.

Sampling procedures are problematic

Because moulds and aflatoxins are not evenly distributed throughout bulk shipments and batches of stored grain, appropriate sampling is critical to get a representative result. Protocols for sampling procedures have been developed, in particular in the context of regulatory control. For instance, in setting maximum levels for aflatoxins, the Codex Alimentarius Commission has specified the protocols to be used for peanuts, almonds, Brazil nuts, hazelnuts and pistachios intended for further processing and for ready-to-eat almonds, Brazil nuts, hazelnuts, pistachios and dried figs. The Food and Agriculture Organization of the United Nations (FAO) has developed a mycotoxin sampling tool which is available on-line¹.

Recommended sampling methods are a problem especially for subsistence farmers in rural areas who do not produce enough grain to spare the quantities needed for accurate testing. Thus there is a need to develop rapid, low-cost, low technology, accurate detection methods for aflatoxins to improve surveillance and control in rural areas. Organizations such as the Partnership for Aflatoxin Control in Africa and the World Food Programme are addressing these issues, e.g. the World Food Programme has instituted the Purchase for Progress Program to ensure grain quality by creating the Blue Box, which contains test kits for grain quality, including aflatoxins.

Aflatoxins can be controlled both pre- and post-harvest

Control measures are required both pre- and postharvest. The most long-term, stable solution to controlling pre-harvest aflatoxin contamination is through enhancing the ability of the crop to resist fungal infection and/or prevent production of aflatoxins by the invading fungus. This can be achieved through plant breeding or through genetic engineering of crops of interest. However, these processes are laborious and time consuming. Effective, sustainable and universally applicable pre-harvest intervention strategies are needed.

One strategy that has received significant attention for reduction of aflatoxins prior to harvest has been biological control using non-toxicogenic *A. flavus* isolates. The non-toxicogenic strains occupy the same niches as the naturally occurring toxicogenic strains, and are capable of competing and displacing the toxicogenic strains. This approach has been deployed on crops such as cotton, maize, peanuts, figs and pistachios in the USA, maize in Africa, and peanuts in Australia, Argentina and China. The strategy has also been used for maize in Thailand to measure the effectiveness of this treatment pre harvest and post harvest; the results were promising, but inconsistent.

Post-harvest interventions include preventive measures to address adequate storage conditions (moisture, temperature, mechanical or insect damage, and aeration), which influence contamination and

¹ <http://www.fstools.org/mycotoxins/>

toxin production by mould. Other measures, such as chemical decontamination or use of enterosorbents, can be used to remove aflatoxins from already contaminated foodstuffs.

Control of aflatoxins requires an integrated approach

Overall, an integrated approach, whereby aflatoxins are controlled at all stages from the field to the table, is required for reduction in risk. Such an approach includes targeted plant breeding practices, enhancement of host plant resistance, and biological control methods, coupled with post-harvest technologies such as proper drying and storage of potentially affected crop products, as well as development of appropriate alternative uses to retain at least some economic return on value of damaged crop.

Therefore by removing the sources of contamination, promoting better agricultural and storage techniques, ensuring adequate resources are available for testing and early diagnosis, enforcing strict food safety standards, informing and educating consumers and (small/subsistence) farmers, promoting better livestock feeding and management, and creating general awareness about personal protection, are some of the ways in which national authorities can help to control aflatoxins.

WHO supports countries in controlling aflatoxins

WHO, in collaboration with FAO, evaluates the science and develops risk assessments to define safe exposure levels. Based on these risk assessments, maximum levels for aflatoxins in different foods are recommended. These form the basis for national regulations to limit contamination.

Since first being noted in the 1960s, aflatoxins have several times been the subject of toxicological evaluation and dietary exposure assessment by the Joint FAO/WHO Expert Committee on Food Additives (JECFA). These evaluations inform the Codex Alimentarius Commission² which has worked, since 1963, to create harmonized international food standards to protect the health of consumers and ensure fair trade practices.

Codex standards set the maximum levels for contaminants and natural toxins such as aflatoxins in food and are the reference for the international trade in food, so that consumers everywhere can be confident that the food they purchase meets agreed standards for safety and quality, no matter where it was produced. The maximum levels for aflatoxins in various nuts, grains, dried figs and milk are in the range of 0.5 to 15 µg/kg (a µgram is one millionths [1×10^{-6}] of a **gram**). To prevent and reduce the risk of aflatoxins in food and feed, Codex has also developed codes of practice, which detail appropriate preventive measures.

In support of this work, WHO collects food contamination data from nationally recognized institutions through the Food Contamination Monitoring and Assessment Programme of the WHO Global Environment Monitoring System, commonly known as GEMS/Food³. The GEMS/Food contaminants database informs governments, the Codex Alimentarius Commission and other relevant institutions, as well as the public, on levels and trends of contaminants in food.

The GEMS/Food programme has also developed a Consumption Cluster Diets database, which provides an overview of food consumption patterns worldwide, through 17 dietary patterns (based on population food choices) covering more than 180 countries. These estimates, together with reported contamination levels, allow assessment of the potential exposure of populations to contaminants such as aflatoxins in food. The consumption diets are based on Food Balance Sheet (FBS) data collected by FAO, and are routinely used by international risk assessment bodies.

National authorities are developing regulations to limit contamination

Exposure to aflatoxins needs to be kept as low as possible to protect the consumer. Many countries have regulations governing aflatoxins in food with prescribed acceptable limits, and most have maximum permitted or acceptable levels for different foodstuffs. Aflatoxins damage health and business opportunities, and importing countries are imposing increasingly more stringent regulations.

² a joint intergovernmental body of FAO and WHO with 187 member states and one member organization (EU): <http://www.codexalimentarius.org>

³ http://www.who.int/foodsafety/areas_work/chemical-risks/gems-food/en/

The Codex recommendations, maximum levels, and codes of practices mentioned above, serve as guidance for national authorities.

The consumers can do

Mouldy foods are potentially contaminated with aflatoxins and therefore are possibly harmful when consumed. The moulds do not just grow on the surface but penetrate deep into food. To reduce exposure to aflatoxins, the consumer is advised to:

- ◆ carefully inspect whole grains and nuts for evidence of mould, and discard any that look mouldy, discoloured, or shriveled;
- ◆ buy grains and nuts as fresh as possible; that have been grown as close to home as possible, and which have not been transported over a long time;
- ◆ buy only reputable brands of nuts and nut butters – aflatoxin moulds are not entirely killed by processing or roasting, so can show up in products e.g. peanut butter;
- ◆ make sure that foods are stored properly and are not kept for extended periods of time before being used; and
- ◆ try to ensure his/her diet is diverse; this not only helps to mitigate aflatoxin exposure, but also improves health and nutrition. Consumers who lack dietary diversity need to pay extra attention to minimize the risk of high exposure to aflatoxins. For example, extensive aflatoxin exposure has been reported from areas where people get a major part of their daily calorie intake from maize; this foodstuff is commonly contaminated with aflatoxins and needs to be handled properly both before and after harvest.

Further reading (references)

Evaluation of certain contaminants in food (Eighty-third report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series WHO Technical Report Series, No.1002, 2017.

Evaluation of certain food additives and contaminants (Sixty-eighth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 947, 2007.

Evaluation of certain mycotoxins (Fifty-sixth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 906, 2002.

Evaluation of certain food additives and contaminants (Forty-ninth report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No. 884, 1999.

JECFA report and additional information are available at www.who.int/foodsafety/areas_work/chemical-risks/en/