

# Mycotoxins: Invisible Threats to Food Safety and Public Health

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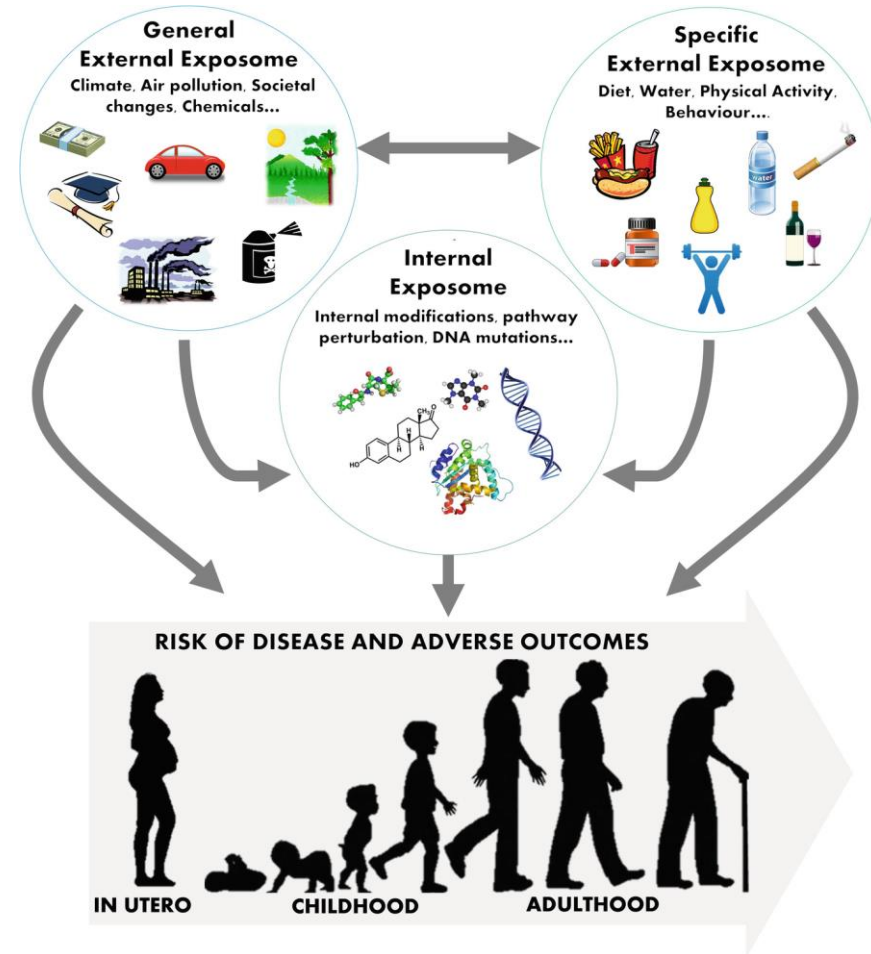
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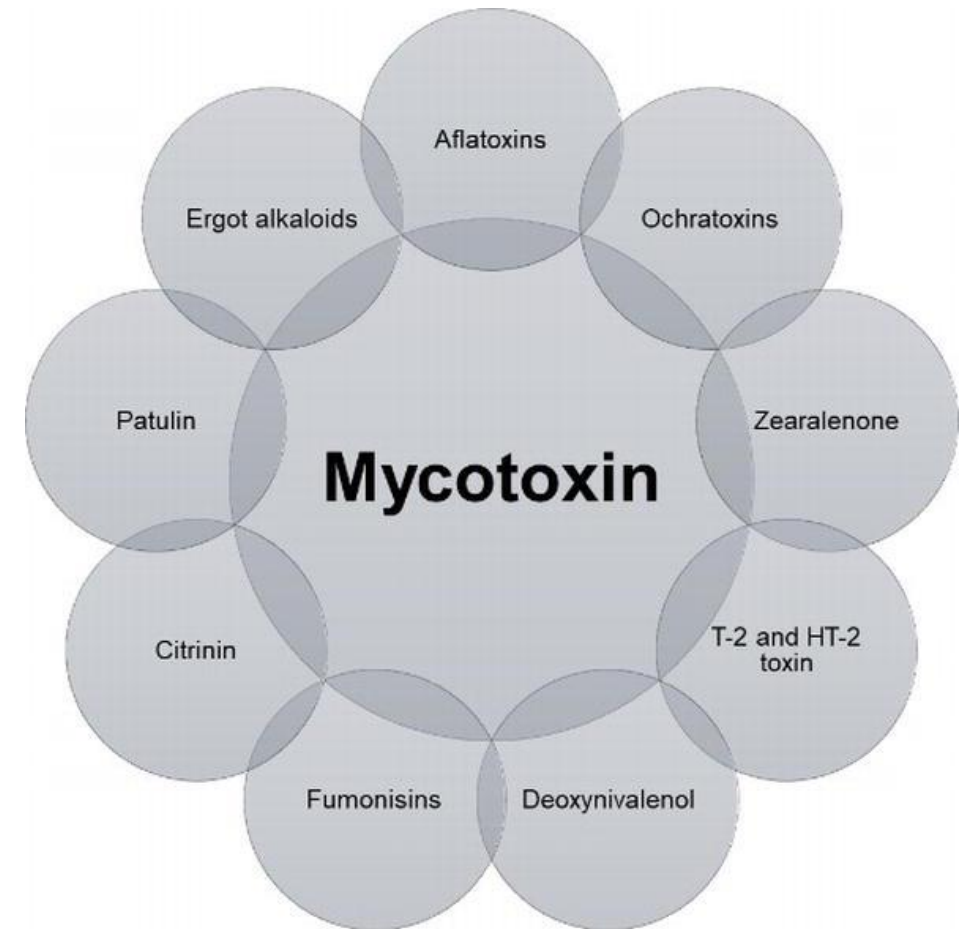
# Exposome

- We are exposed to numerous biological stressors throughout our lifetime
- Can be external or internal
  - Exposome: all of the exposures an individual experiences in their lifetime, and the corresponding health effects that follow
- These exposures have potent, lasting effects on our health
- Diet is a major route of exposure
  - mycotoxins



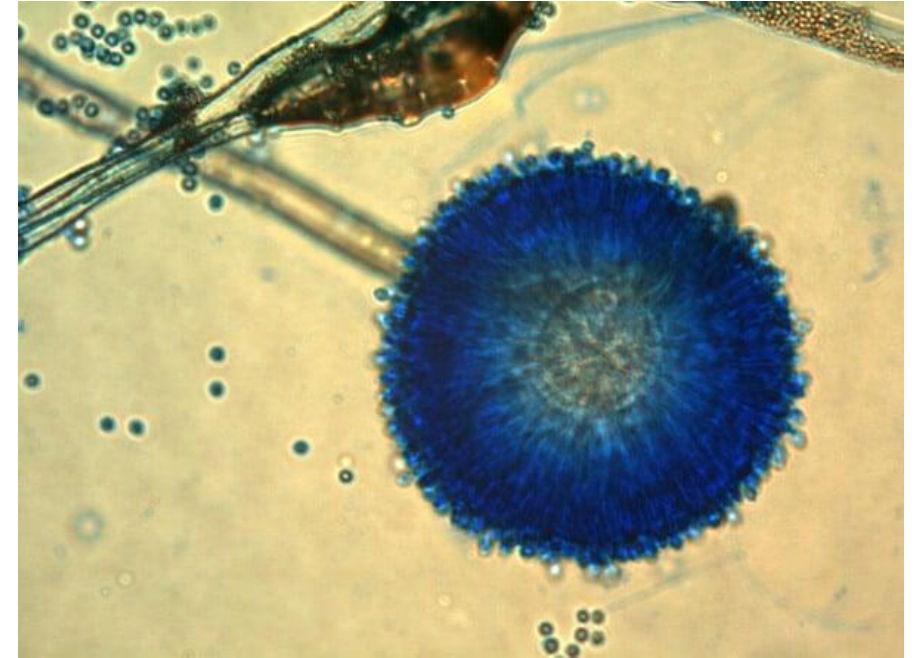
# Mycotoxins

- Mycotoxins are naturally occurring, poisonous compounds
- They are produced by fungi
  - Myco = fungi
- Many classes of mycotoxins produced by many species of fungi
- Mycotoxin-producing fungi are found all over the world and colonize many of our crops, becoming prominent food contaminants
  - Very stable – survive heating, freezing, drying, storage, etc.



# Health effects of mycotoxins

- Mycotoxins have profound effects on human and animal health (mycotoxicosis)
  - Many are carcinogens
- Effects can be acute (immune suppression) or chronic (cancer)
  - Interplay between gut microbiome and mycotoxins
- Time and duration of exposure is also important
  - Many mycotoxins affect child development
- Most governments have regulations in place for allowable amounts of mycotoxins in food
  - Levels are less stringent for animal feed



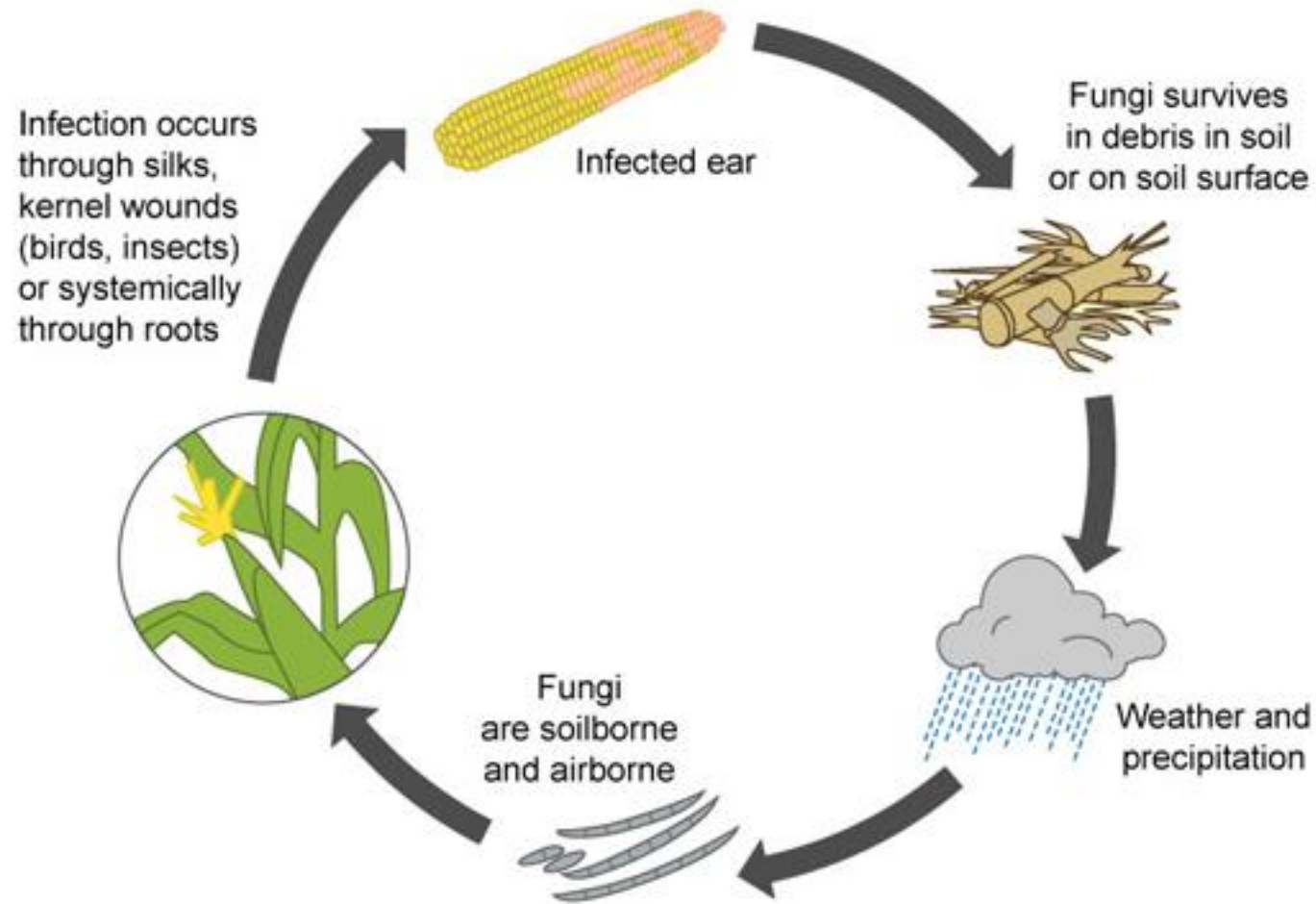
*Aspergillus ochraceus* – a fungus that produces ochratoxins

# Mycotoxin occurrence in foods

- A **wide variety** of food products can be contaminated with mycotoxins
- Main factors affecting contamination:
  - Preference of food substrate for fungus
  - Temperature (80-100°F)
  - Humidity/heavy rainfall ( $\geq 85\%$  humidity)
  - Pests/crop damage
  - Storage conditions/hygiene practices
- Mycotoxins are **extremely** potent. Have health effects in a part per billion (ppb) range
- Cross contamination is common – not obvious that food is contaminated



# Fungal disease cycle



# Mycotoxin occurrence in foods

**Table 1** Mycotoxins of public health concern, associated fungi, and food/feed crops at risk of contamination

<b>Mycotoxin</b>	<b>Producing fungi</b>	<b>Associated food/feed crops</b>
Aflatoxins	<i>Aspergillus flavus</i> <i>A. parasiticus</i>	Maize, peanuts, tree nuts, copra, spices, cottonseed
Fumonisin	<i>Fusarium verticillioides</i> <i>F. proliferatum</i> <i>A. niger</i>	Maize
Trichothecene mycotoxins	<i>F. graminearum</i> <i>F. culmorum</i>	Maize, wheat, barley, oats
Ochratoxin A	<i>Penicillium verrucosum</i> <i>A. ochraceus</i> <i>A. carbonarius</i> <i>A. niger</i>	Maize, wheat, barley, oats, dried meats and fruits, coffee, wine

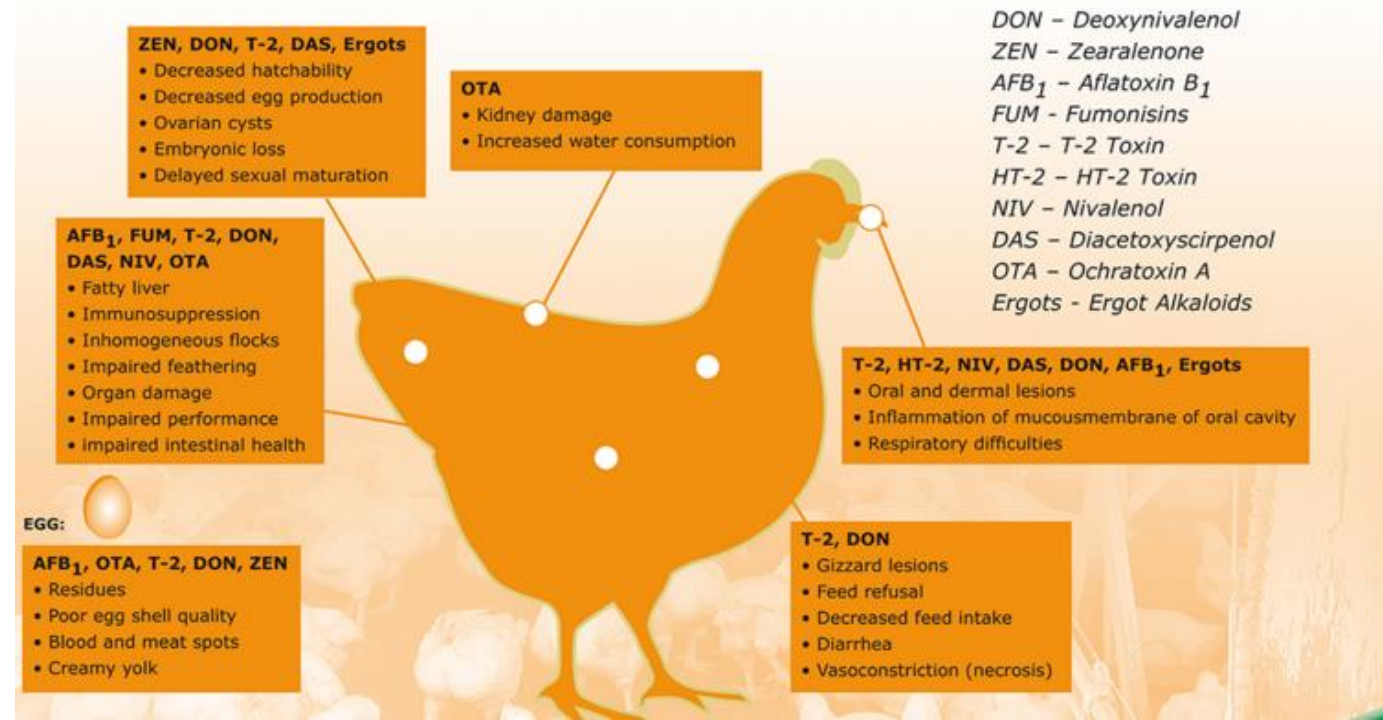
# Contamination in animal feed

- Pet food recalls often due to mycotoxin contamination
- Mycotoxins affect quality of animal products from livestock
- Mycotoxins also travel up the food chain, creating additional routes of human exposure

## FDA Alert: Certain Lots of Sportmix Pet Food Recalled for Potentially Fatal Levels of Aflatoxin

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### Effects of Mycotoxins



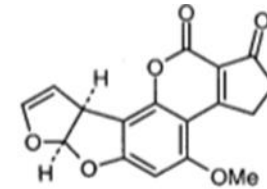


# Economic impact of mycotoxins

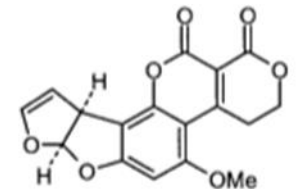
- Contamination has significant economic impacts on the agricultural industry
- Estimated that 25% of the world's crops are affected by mycotoxins each year
  - Annual losses of ~1 billion metric tons of food and food products
- Loss estimates vary, but U.S. is estimated to lose \$0.5 to \$1.5 billion per year
- Economic losses due to:
  - Reduce crop value/crop destruction
  - Losses in animal productivity due to mycotoxin-related health problems
  - Human health costs
  - Testing/prevention/litigation

# Aflatoxins

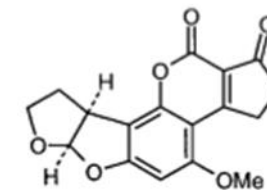
- Four major aflatoxins produced by *Aspergillus*:
  - B<sub>1</sub>, B<sub>2</sub>, G<sub>1</sub>, G<sub>2</sub>
- Found on many staple foods (rice, corn, groundnuts, spices, etc.)
- Relative toxicity: AFB<sub>1</sub> >> AFG<sub>1</sub> > AFB<sub>2</sub> > AFG<sub>2</sub>
- AFB<sub>1</sub> is a class 1 carcinogen
  - leads to the development of hepatocellular carcinoma (HCC)
    - Up to 28% of all cases – synergism with HBV



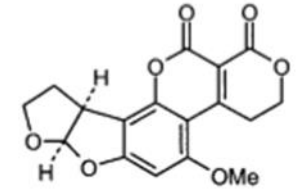
AFB<sub>1</sub>



AFG<sub>1</sub>



AFB<sub>2</sub>



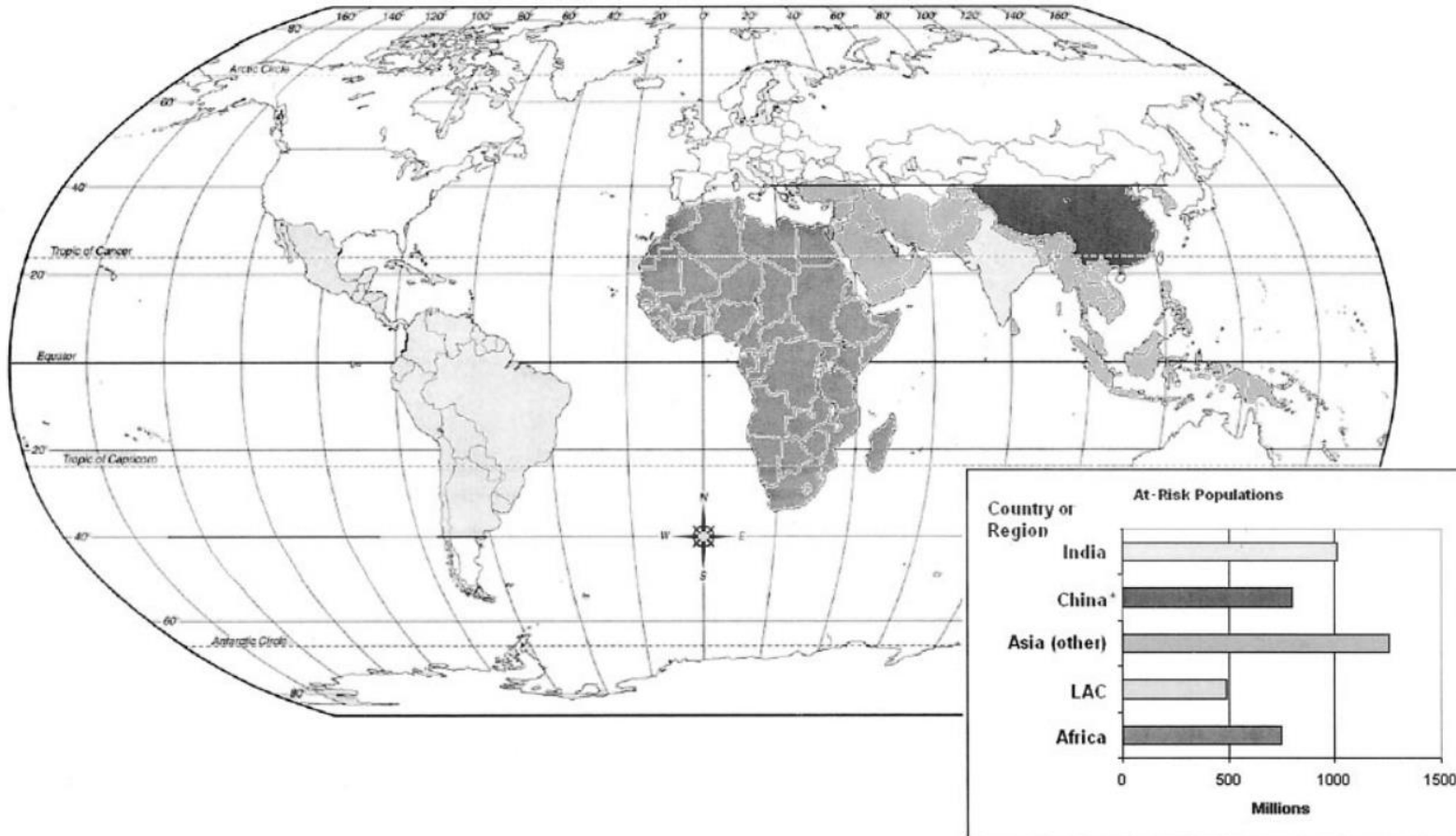
AFG<sub>2</sub>

# Turkey X Disease

- Event in the early 1960s that lead to aflatoxin discovery
- Death of over 100,000 turkeys in England was traced back to contaminated peanut meal from Brazil
- Sparked great interest into mycotoxin research



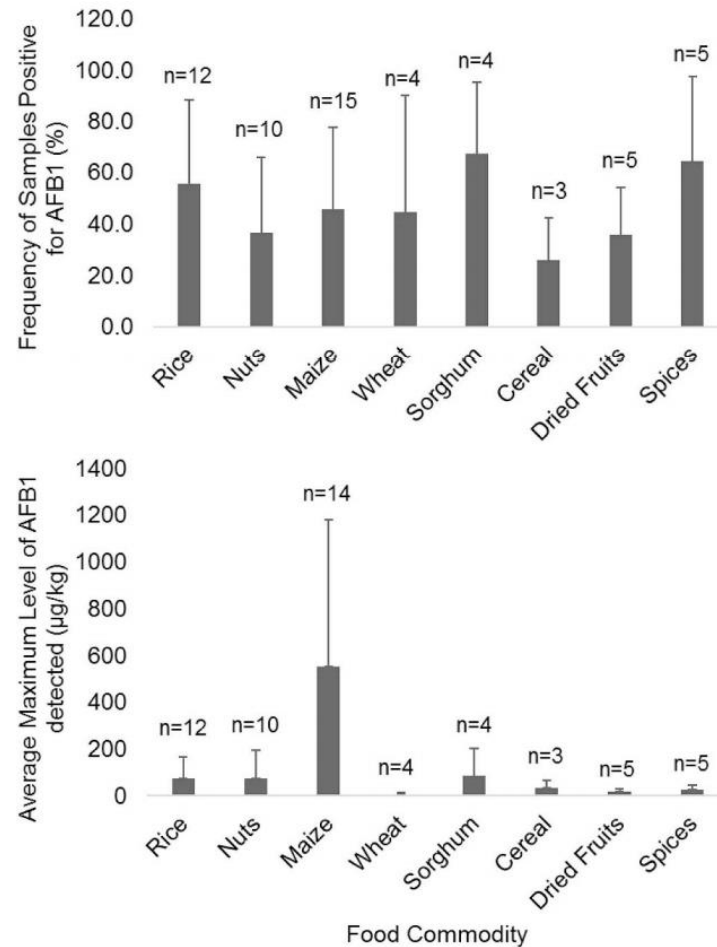
# Geographical Risk of Aflatoxin Exposure



Kenya – 2004 outbreak –  
317 deaths from acute exposure

\* Estimated 66% of 1.2 billion people

# Aflatoxin levels can be found well above acceptable limits



**U.S. limit for AFB1 is 20 ppb for human consumption**

# Occupational exposures of aflatoxins

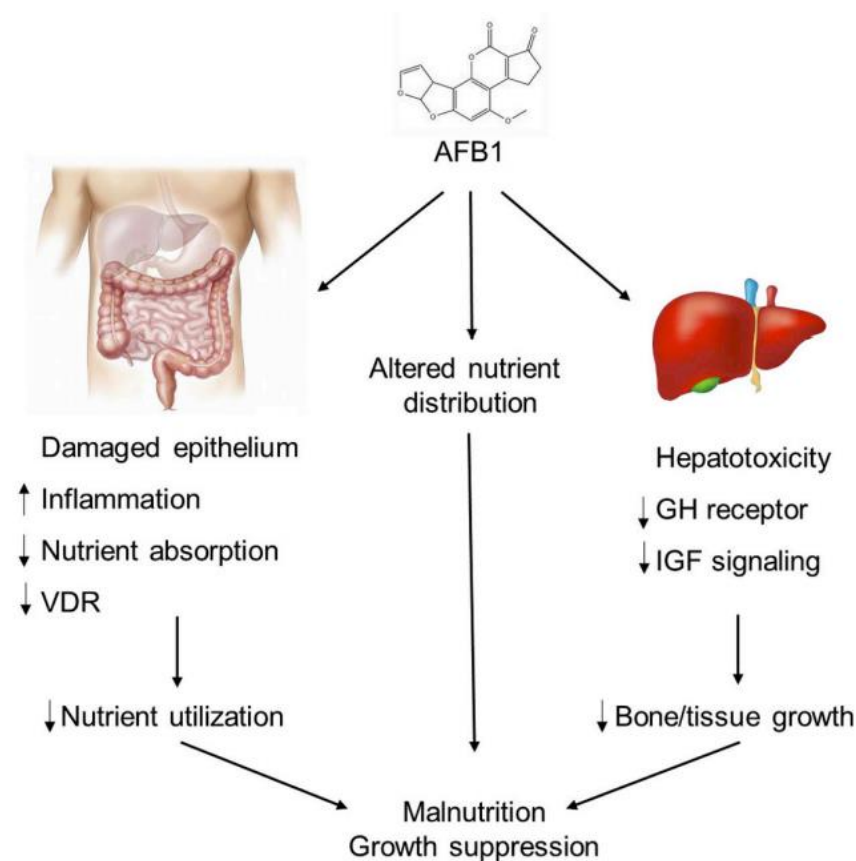
- Occupations in the agricultural industry can lead an individual to have additional risks of aflatoxin exposure
- Breathing in aflatoxin-containing particulates (corn dust) is a major source of occupational exposure

## Reports of occupational exposure to AFB1

Country	Occupation
Netherlands	oilpress
Sweden	grain millers
Denmark	animal feed
Denmark	animal feed
Portugal	poultry production
Nigeria	feed mill workers
Egypt	textile workers
Portugal	swine production
Portugal	poultry and swine production
Portugal	waste management
India	food-grain workers
Egypt	wheat handlers
China	sugar and papermaking workers
Portugal	slaughterhouse
Italy	feed production and sorting

# Toxicology of Aflatoxins

- Aflatoxins (particularly AFB1) are genotoxins → DNA damaging agents
- AFB1 is metabolized primarily by the liver into its toxic form which reacts with DNA and other cellular components
- This leads to multiple detrimental health effects
  - Liver cancer
  - Malnutrition
  - Growth suppression – exposure through breast milk
  - Modulation of the immune system
- Can cause nutritional deficiencies by altering nutrient absorption/utilization



# Toxicology of Mycotoxins

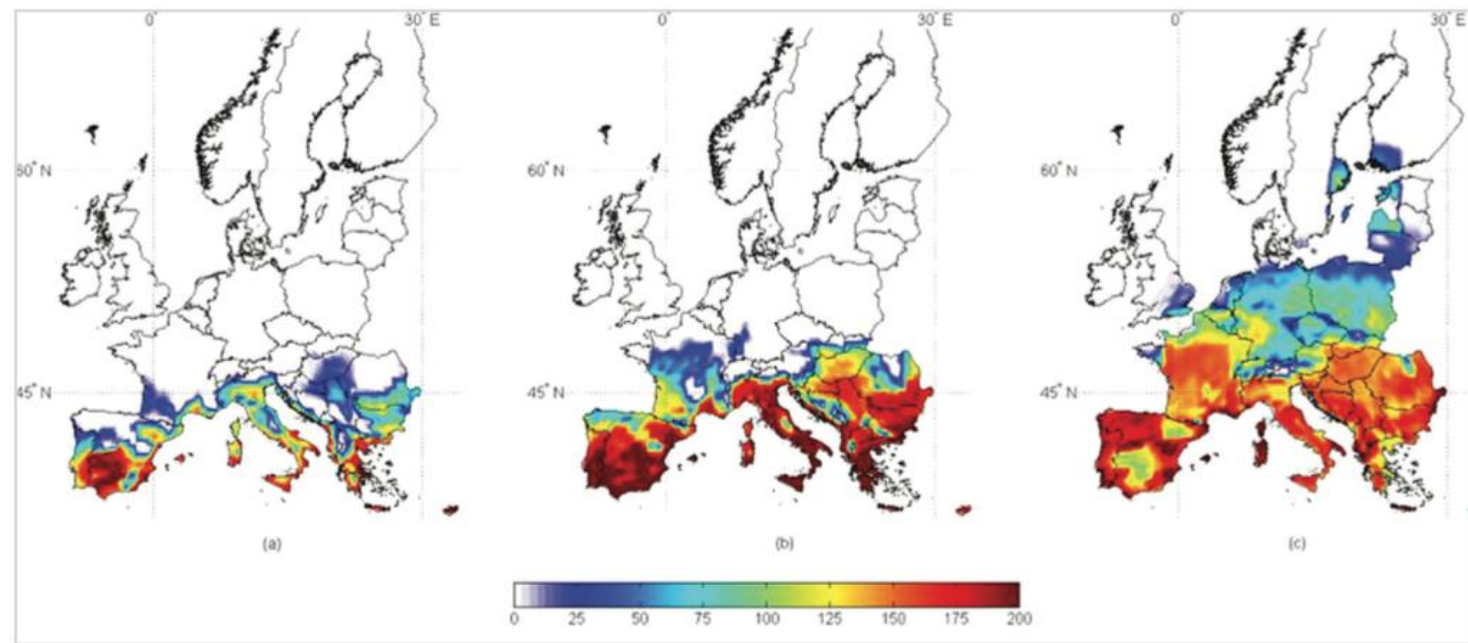
*Table 1.* Organ toxicity secondary to mycotoxins.

Organ toxicity	Mycotoxins	Proposed mechanism	Comments
Pulmonary hemorrhage	Trichothecenes	Protein and collagen synthesis inhibition	High levels of airborne toxin needed
Encephalopathy	Aflatoxins	Cytotoxicity	Consumption of toxins
	Ergot alkaloids	Vasoconstriction	
CNS depression	Microbial volatile organic chemicals (complex alcohols and aldehydes)	Decrease activity of CNS neurons similar to alcohols and aldehydes	Sufficient/exceed concentrations to induce mucous membrane irritation
Hematologic/immunologic Suppression	Trichothecenes	Protein and enzyme synthesis inhibition	High levels of airborne toxin needed or consumed
Cancer	Aflatoxins		
Liver	Aflatoxins	Electrophilic binding of DNA/RNA nucleophilic sites	Consumption of mycotoxin-contaminated food
Esophageal	Fumonisin		
Nephropathy	Ochratoxins	Direct cytotoxicity	Consumption of food contaminated with mycotoxins
Teratogenicity	Ergots	Binding of nucleophilic sites	Consumption of mycotoxin-contaminated food
	Trichothecenes		
	Aflatoxins		
Gastrointestinal toxicity	Most mycotoxins	Direct cytotoxicity	Consumption of mycotoxin



# Climate change is expected to increase mycotoxin occurrence

Risk maps for aflatoxin contamination in maize at harvest in 3 different climate scenarios, present, +2 °C, +5 °C

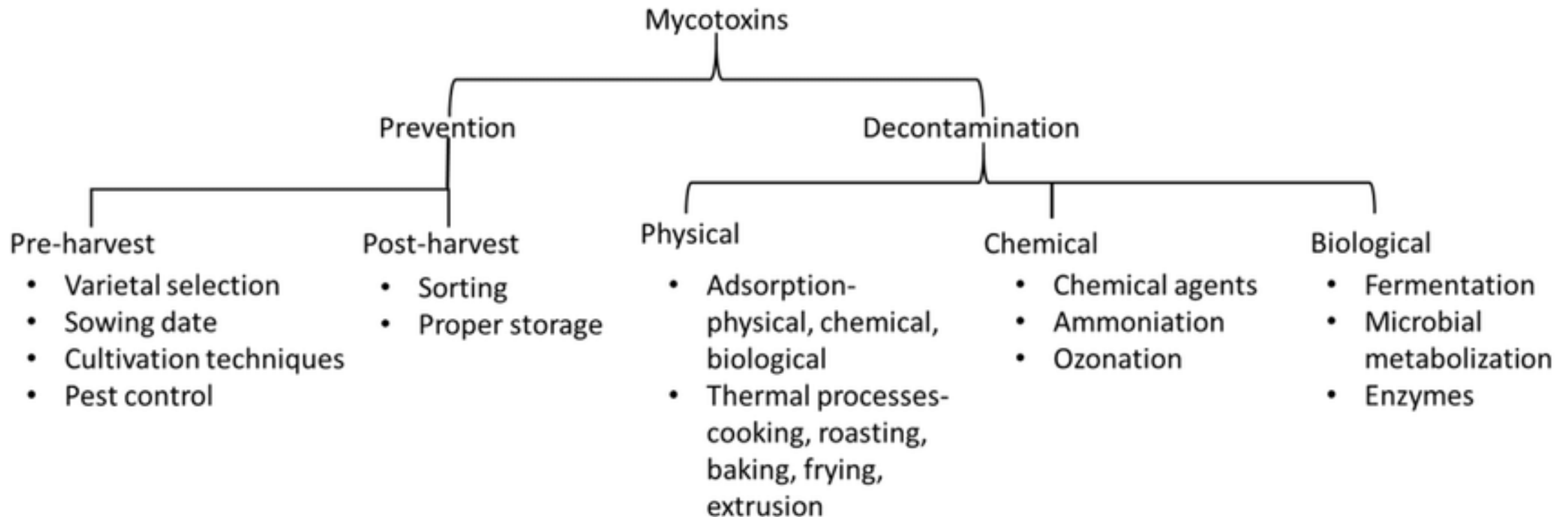


Source: Battilani et al. (2016)<sup>21</sup>

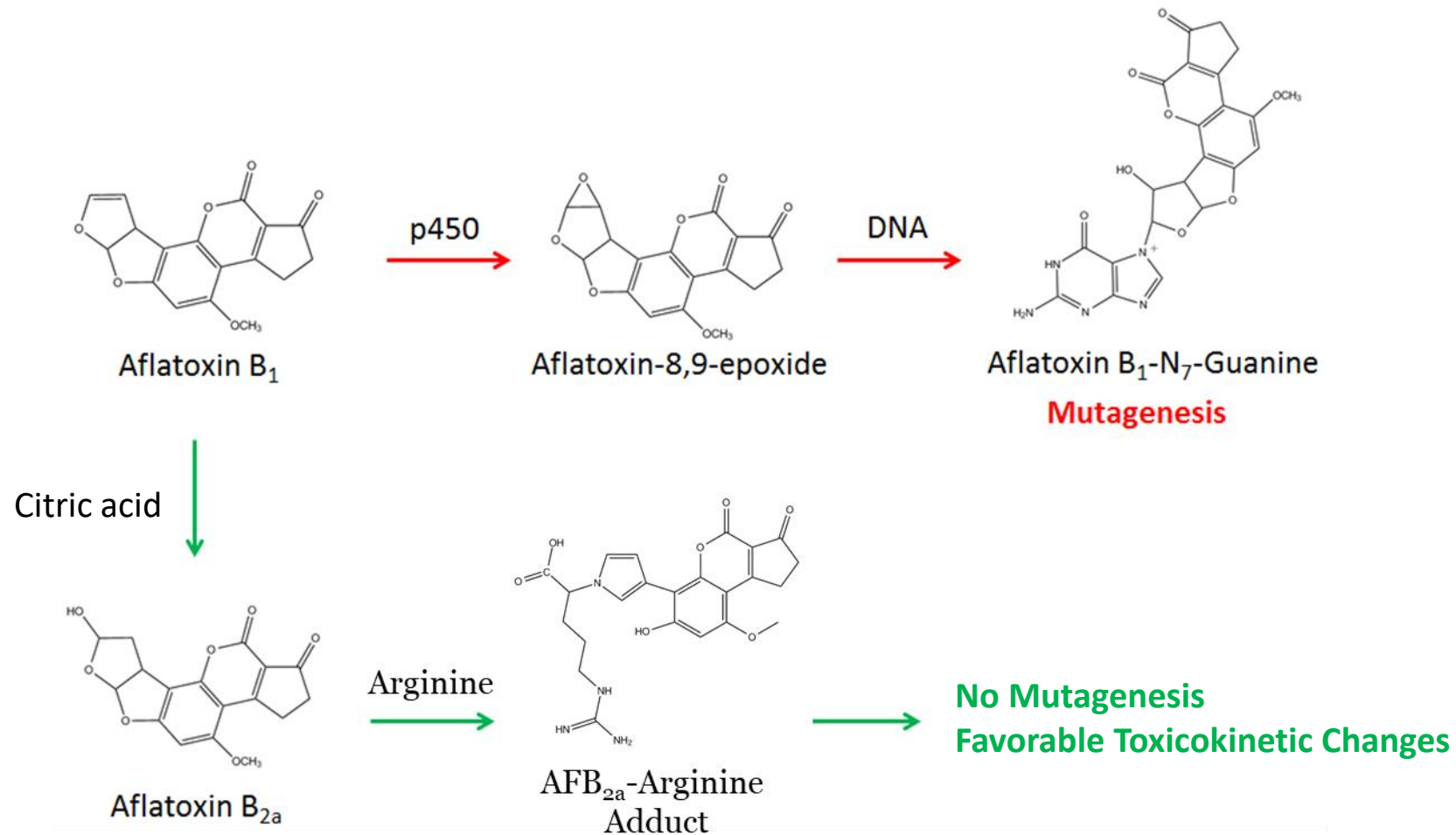
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- As climate change becomes more severe, many countries are expected to see an increased burden of mycotoxin occurrence

# Mitigation of Mycotoxins

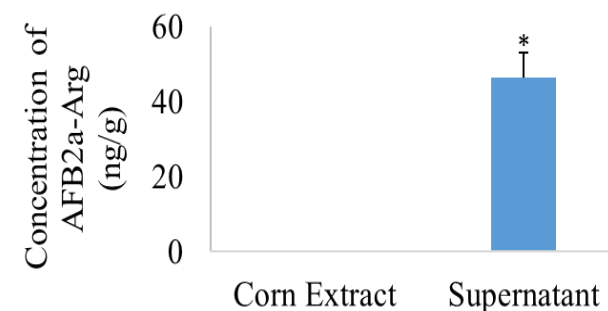
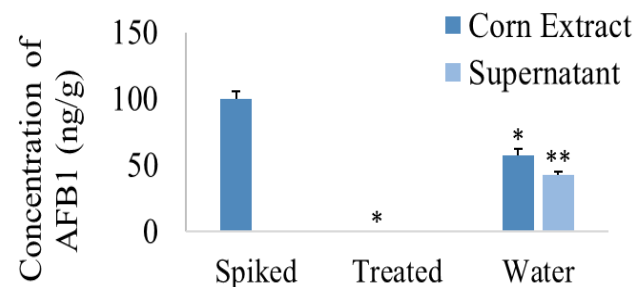
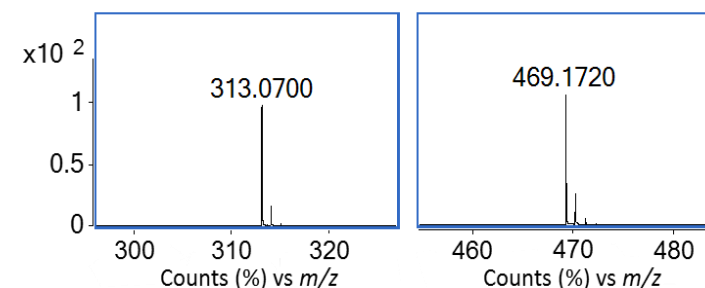
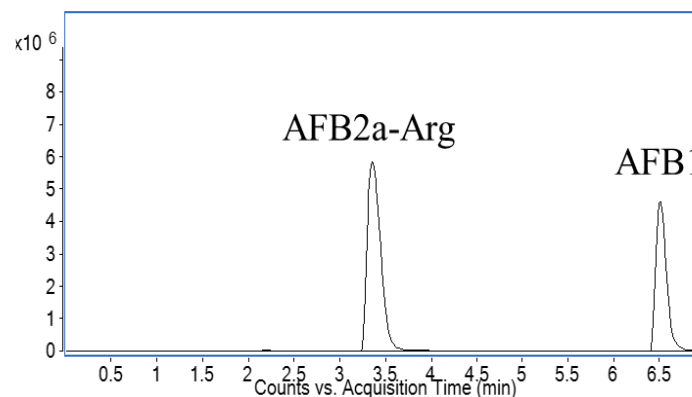


# Novel Decontamination Methods for AFB1



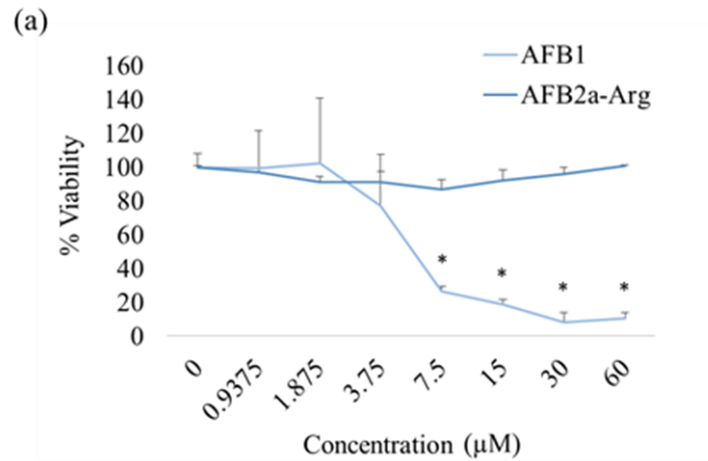
# Transformation of AFB1 on corn

- Treatment reduced AFB1 below detectable levels
- Newly formed adduct was found only in the treatment solution

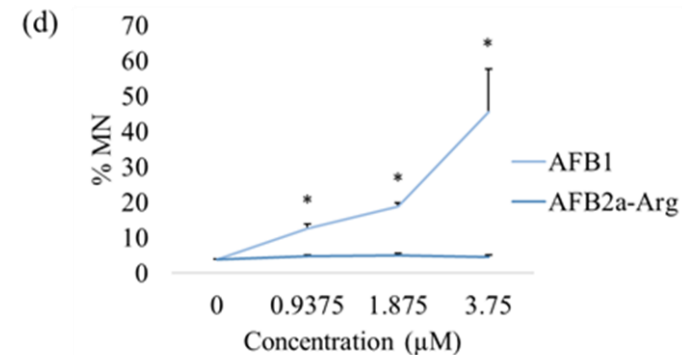
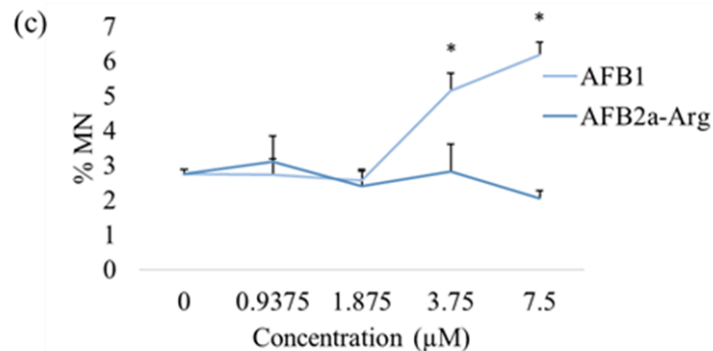
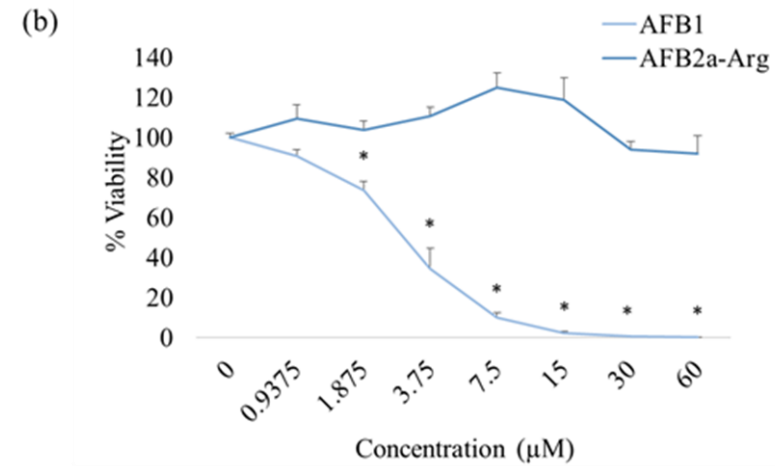


# Modification of AFB1 reduces toxicity

## HepG2



## HepaRG



# Cooking methods to remove mycotoxins

- Certain cooking methods are effective at reducing mycotoxin levels
- Making tortilla involves a process known as nixtamalization, which involves soaking and cooking corn or other grains in an alkaline solution (usually limewater)
  - This process has shown to be highly effective at removing aflatoxins (up to 97%)
- Roasting peanuts also has been shown to degrade significant amounts of aflatoxins ~50-90%



# Concluding remarks

- Mycotoxins pose significant health risks, but there are steps that can be taken to reduce exposure:
  - inspect whole grains for evidence of mold, and discard any that look moldy, discolored, or shriveled
  - avoid damage of grains before and during drying, and in storage, as damaged grain is more prone to invasion of molds/mycotoxins
  - buy grains and nuts as fresh as possible
  - make sure that foods are stored properly – kept free of insects, dry, and not too warm
  - Don't keep foods for extended periods of time before being used
  - ensure a diverse diet – this not only helps to reduce mycotoxins exposure, but also improves nutrition.