Fish Health Management Workshop: North-South Dialogue on Capacity Building and Knowledge Transfer Approaches

19th – 24th Sept, 2022, Kisumu Hotel, Kenya

Addressing Global Food Security Challenges through Partnerships and Local Community Engagement

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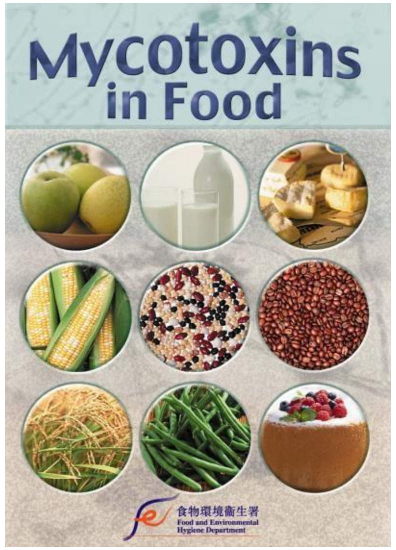

MYCOTOXINS: WHAT ARE THEY AND HOW DID THEY GET THERE?

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September 25, 2022

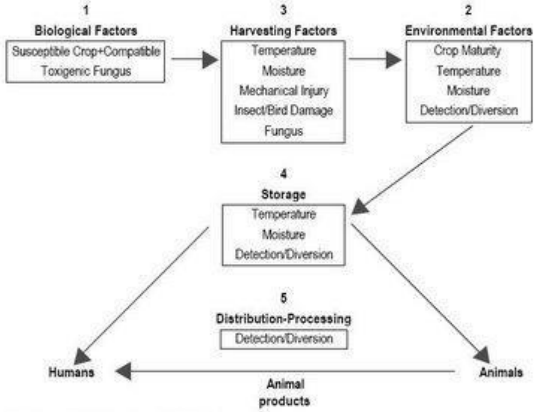
OUTLINE

I. Types of mycotoxins
II. Economic impacts
III. Health impacts
IV. Regulation of mycotoxins in the food/feed supply
V. Factors influencing occurrence of mycotoxins
VI. Determining mycotoxin levels
VII. Management strategies

Mycotoxins

- Secondary metabolites produced by fungi that are toxic to animals
  - More than 300 known
  - Natural contaminants; most are chemically stable
- First identified with Turkey X Disease
- Alternative uses: antibiotics, biological reagents, chemical weapons, etc.

Image courtesy of NBC News.com



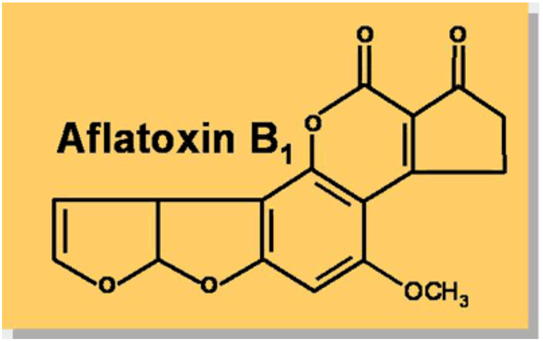
Mycotoxins in human nutrition and health 1994,
adapted from J.E.Smith, G.L.Solomons, C.W.Lewis & J.G. Anderson, European Commission DGXII

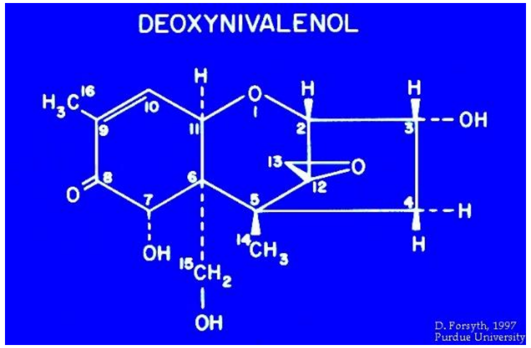
II. Economic impacts

- Direct and indirect costs
  - Yield loss to disease
  - Reduced crop value
  - Losses in animal productivity
  - Human health costs
  - Management
    - Prevention
    - Sampling/testing
    - Mitigation
    - Litigation
    - Research

I. Types of mycotoxins

Mycotoxin	Causal agent	Affected crops
Aflatoxins	*Aspergillus flavus*, *A. parasiticus*	**Corn**, cottonseed, **peanut**, tree nuts, sorghum
Deoxynivalenol (DON, vomitoxin)	*Gibberella zeae* (*Fusarium graminearum*)	**Corn**, **wheat**, **barley**, sorghum
Zearalenone	*Gibberella zeae* (*Fusarium graminearum*)	Corn, sorghum
Fumonisin	*Fusarium verticillioides*, *Fusarium* spp.	Corn, sorghum





Mycotoxins

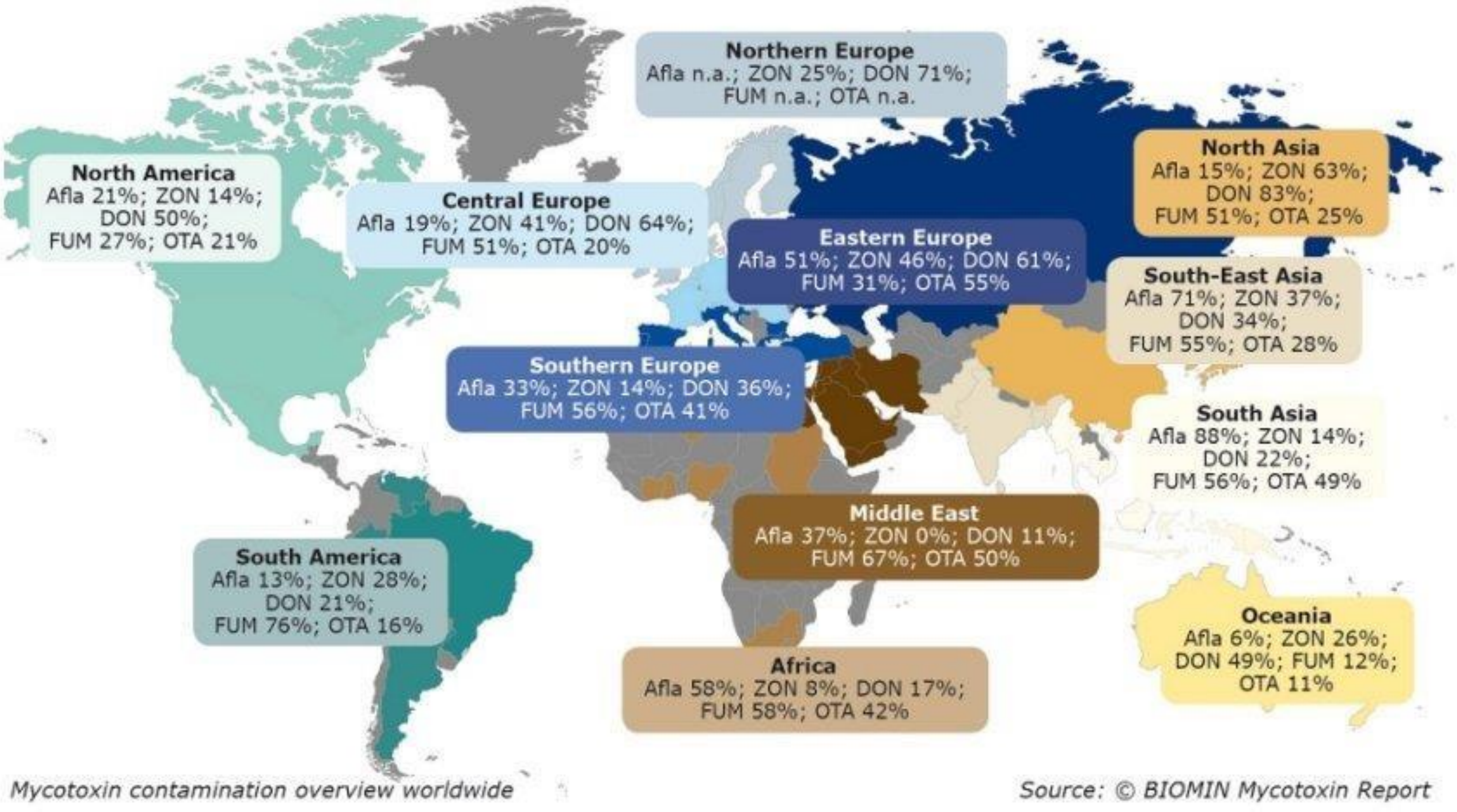
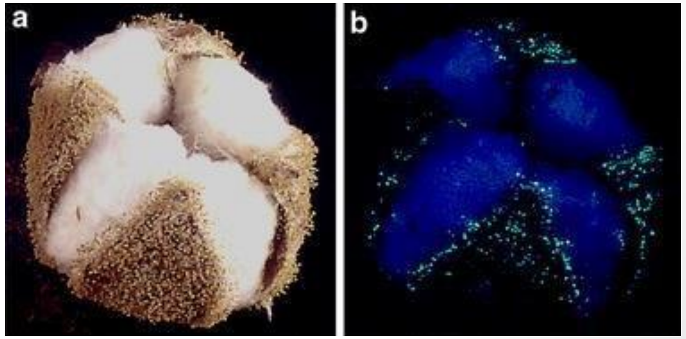


Figure courtesy of [VET-Magazin]

Aspergillus flavus

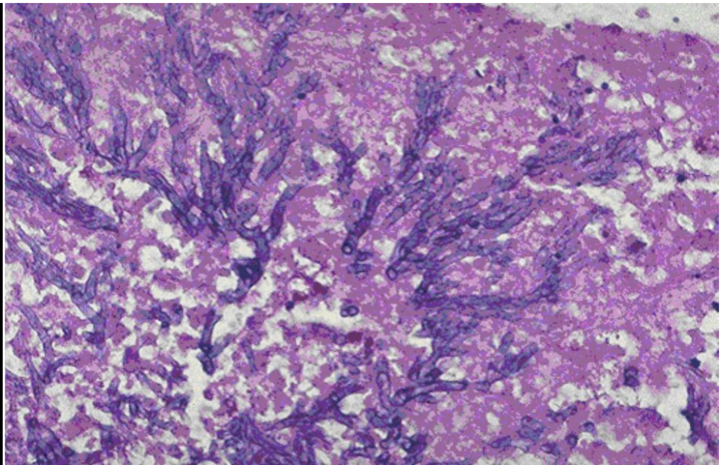
- Fungus in Ascomycota phylum
- A common saprophyte within the soil but does cause disease on corn, peanut and cotton
- Also a common pre- and post-harvest contaminant
- Produces aflatoxins (secondary metabolites that are toxic to animals); B1 induces immunosuppression in chickens, lab rats, etc.

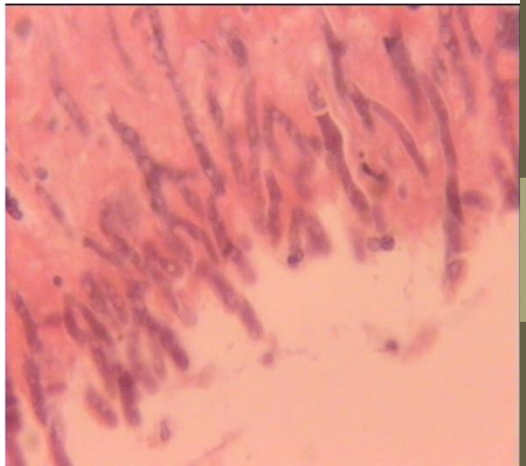


Images courtesy of Pioneer, APS*net* and Mycopathologia websites

Aspergillus flavus

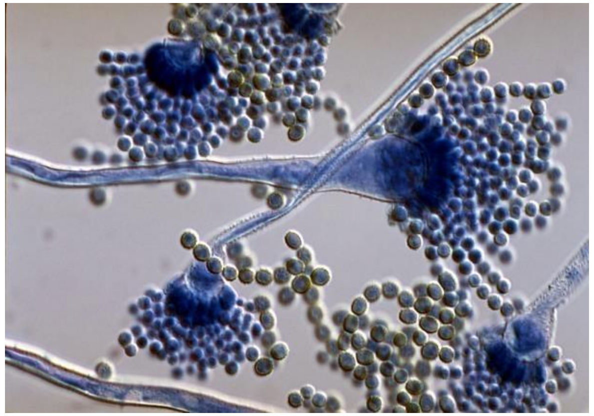
- Second leading cause of invasive aspergillosis
  - Can become a systemic infection and lead to death
- Also causes keratitis, endocarditis and cutaneous, urinary tract and central nervous system infections
- Treatment involves antifungal drugs; prognosis for invasive aspergillosis is generally poor

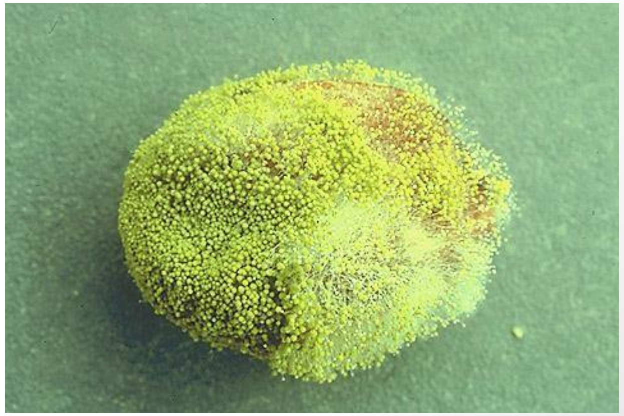




Mycotoxins - Aflatoxin

- Produced by *Aspergillus flavus* and *A. parasiticus*
- 14 different types of aflatoxin
  - B_1 considered most toxic / potent
- Host crops include corn, peanuts and soybean
- Environmental conditions affect toxin production
  - High moisture and high temperature

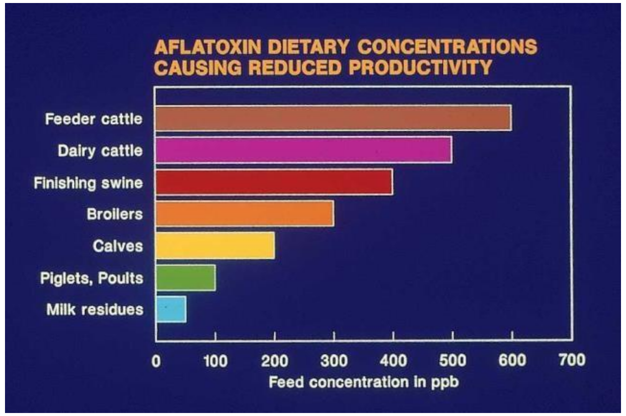




Images courtesy of Illinois.edu and APS*net* websites

Mycotoxins - Aflatoxin

- Toxins target the liver, causing cirrhosis and cancer
- Can be passed through milk (dairy or human)
- Allowable concentration regulated by FDA
  - Depends on human food or animal feed
- Recent U.S. recalls include: peanut butter, grits and pet food

Images courtesy of The Milk Run and Cagle websites

Mycotoxins - Trichothecenes

- Produced by *Fusarium* spp.
- 40 different types of trichothecene
  - Deoxynivalenol (DON or vomitoxin) and T-2
  - Some (like T-2) can be absorbed through the skin
- Host crops include: wheat, barley, rice and corn
- Favored by high moisture and low temperature



Images courtesy of UW Extension and IA State.edu websites

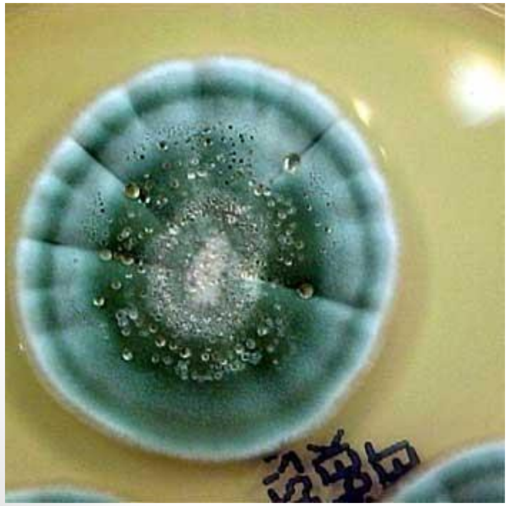
Mycotoxins - Trichothecenes

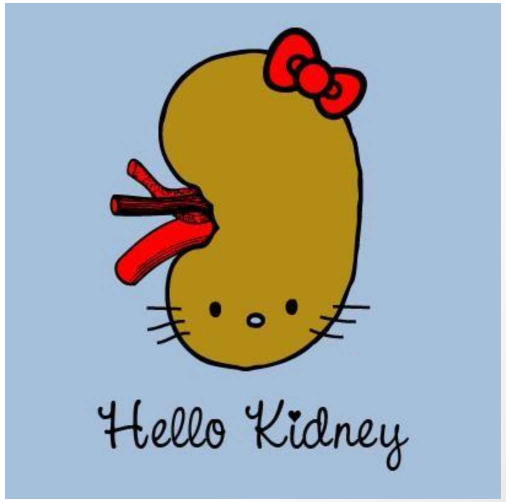
- Toxins target gastrointestinal tract
  - Inhibit protein, RNA and DNA synthesis
  - Also cause hemorrhages and immunosuppression
- Allowable concentration regulated by FDA
  - Depends on human food or animal feed
- Recent global recalls include: oat rolls, oatmeal, and couscous

Images courtesy of Quicking.cn and Med.Utah.edu websites

Mycotoxins - Citrinin

- Produced by *Penicillium* and *Aspergillus* spp.
- Toxin targets the kidneys
  - Can be absorbed through the skin
  - Associated with Balkan endemic nephropathy
- Host crops include: oat, wheat, rye and rice





Images courtesy of UMN.edu and EU Risk Consulting websites

I. Types of mycotoxins

Aspergillus ear rot

Fusarium ear rot
(Courtesy G. Munkvold)

Gibberella ear rot
(Courtesy G. Munkvold)

Aspergillus pod rot

Aspergillus boll rot
(Courtesy P. Cotty)

Fusarium head blight
(Courtesy C. Griffey)

III. Health impacts - humans

- **Aflatoxins**
  - Liver cancer
  - Stunting
  - Reproductive problems
  - Immune suppression
  - Death (acute hepatitis)
- **Deoxynivalenol (vomitoxin)**
  - Nausea and vomiting
  - Fever, headaches
- **Zearalenone**
  - Mimics estrogen
- **Fumonisin**
  - Esophageal cancer
  - Neural tube birth defects

➢ Monitoring and regulation of mycotoxins in the food supply minimizes exposure and human health impacts in developed countries (but imposes an economic burden).

➢ Acute and chronic exposure to mycotoxins imposes a significant health burden in developing countries.

IV. Regulation in food/feed

- **United States Food and Drug Administration (U.S. FDA)**
- **Advisory levels** provide guidance to industry concerning levels of a substance present in food or feed that are believed to provide an adequate margin of safety to protect human and animal health.
- **Action levels** specify a precise level of contamination at which the agency is prepared to take regulatory action.

- **Aflatoxins** – action levels
- **Deoxynivalenol (vomitoxin)** – advisory levels
- **Zearalenone** – no established levels
- **Fumonisin** – advisory/guidance levels

- International markets have their own standards (lower limits)
- Individual grain buyers may have a lower tolerance for mycotoxins

IV. Regulation in food/feed

U.S. FDA action levels for aflatoxins

Product	Aflatoxin, ppb
All products, except milk, for human consumption	**20 ppb**
Corn for immature animals and dairy cattle	**20 ppb**
Corn and peanut products for breeding beef cattle, breeding swine, or mature poultry	**100 ppb**
Corn and peanut products for finishing swine	**200 ppb**
Corn and peanut products for finishing beef cattle	**300 ppb**
All other feedstuffs	**20 ppb**
Milk	**0.5 ppb**

IV. Regulation in food/feed

U.S. FDA advisory levels for DON

Product	DON, ppm
All finished wheat products for human consumption	**1 ppm**
Ruminating beef, feedlot cattle, chickens	**10 ppm in <50% of diet**
Swine	**5 ppm in <20% of diet**
All other animals	**5 ppm in <40% of diet**

*Dried distillers' grain and solubles (DDGS), co-products of ethanol production, have increased levels of mycotoxins

IV. Regulation in food/feed

U.S. FDA advisory/guidance levels for fumonisin

Product	Fumonisin, ppm
Corn products for human consumption	2-3 ppm
Equids and rabbits	5 ppm, <20% of diet
Swine and catfish	20 ppm, <50% of diet
Breeding ruminants, breeding poultry	30 ppm, <50% of diet
Ruminants >3 months old and fed for slaughter	60 ppm, <50% of diet
Poultry fed for slaughter	100 ppm, <50% of diet
All others (includes dogs and cats)	10 ppm, <50% of diet

V. Factors influencing occurrence

- **Disease signs/symptoms ≠ mycotoxin contamination**
- Dependent on:
  - Mycotoxin-producing potential of the fungus (variable between and within species)
  - Environmental conditions conducive to mycotoxin production

V. Factors influencing occurrence

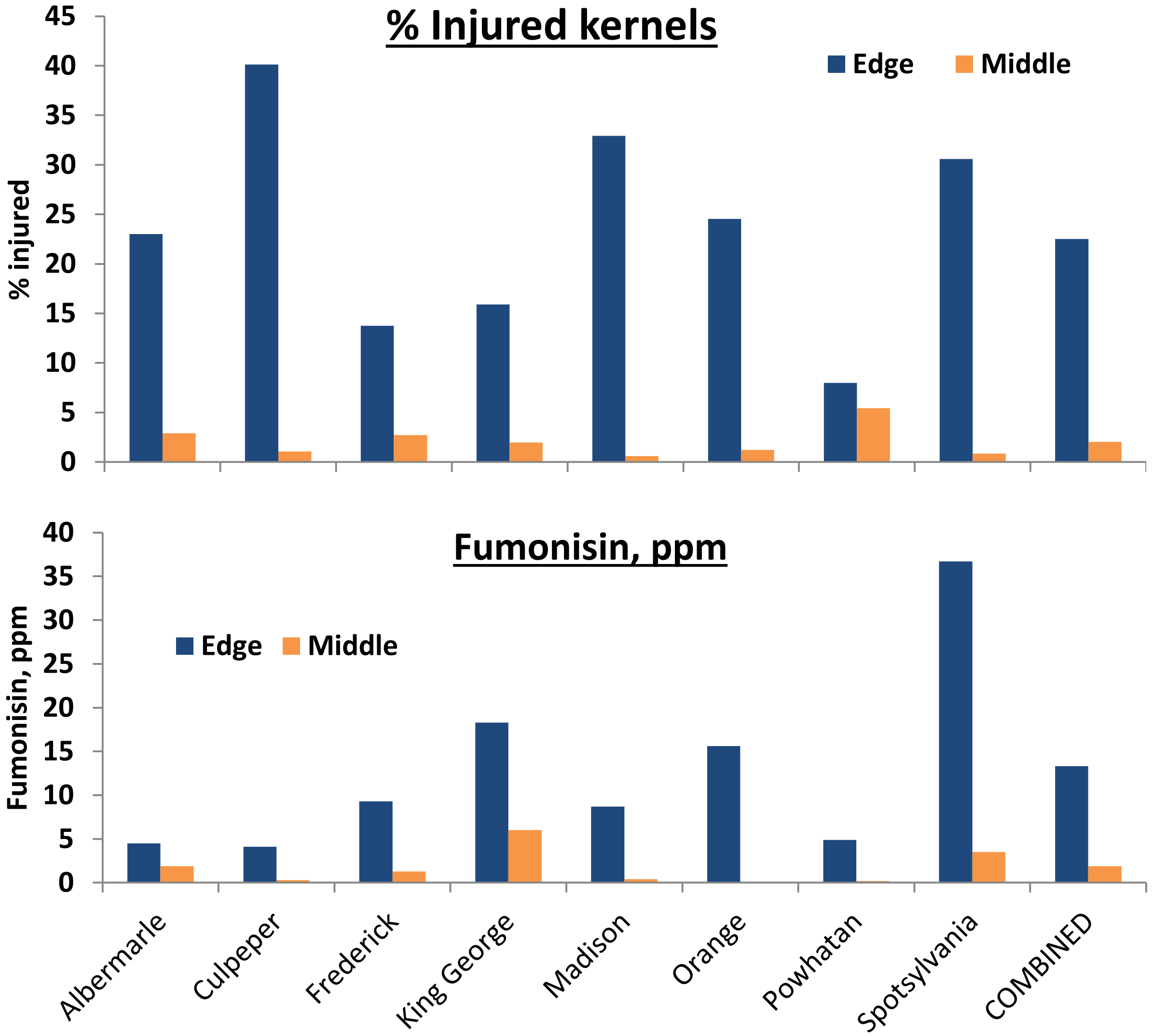
Fungus	Mycotoxin	Optimum temperature (°F)	Moisture
Aspergillus flavus	**Aflatoxin**	80-100	High grain moisture but severe drought stress
Gibberella zeae (Fusarium graminearum)	**DON**	70-85	High humidity (> 90% RH)
	Zearalenone	65-85	High humidity (> 90% RH)
Fusarium verticillioides	**Fumonisin**	80-100	Drought stress followed by wet weather (> 85% RH)

V. Factors influencing occurrence

- **Abiotic stress**
  - Drought stress
  - Poor fertility
- **Biotic stress**
  - Insect damage

Brown marmorated stink bug injury & mycotoxins

V. Factors influencing occurrence



Fumonisin vs BMSB damage:
r^2 = 0.26, P = 0.0004

V. Factors influencing occurrence

Two phases of contamination

- **Phase 1 -** crop development
  - Dependent on epidemiology of disease

- **Phase 2 -** following maturation, field & post-harvest
  - Warm, humid conditions
  - Low levels of contamination in field can result in high levels in storage

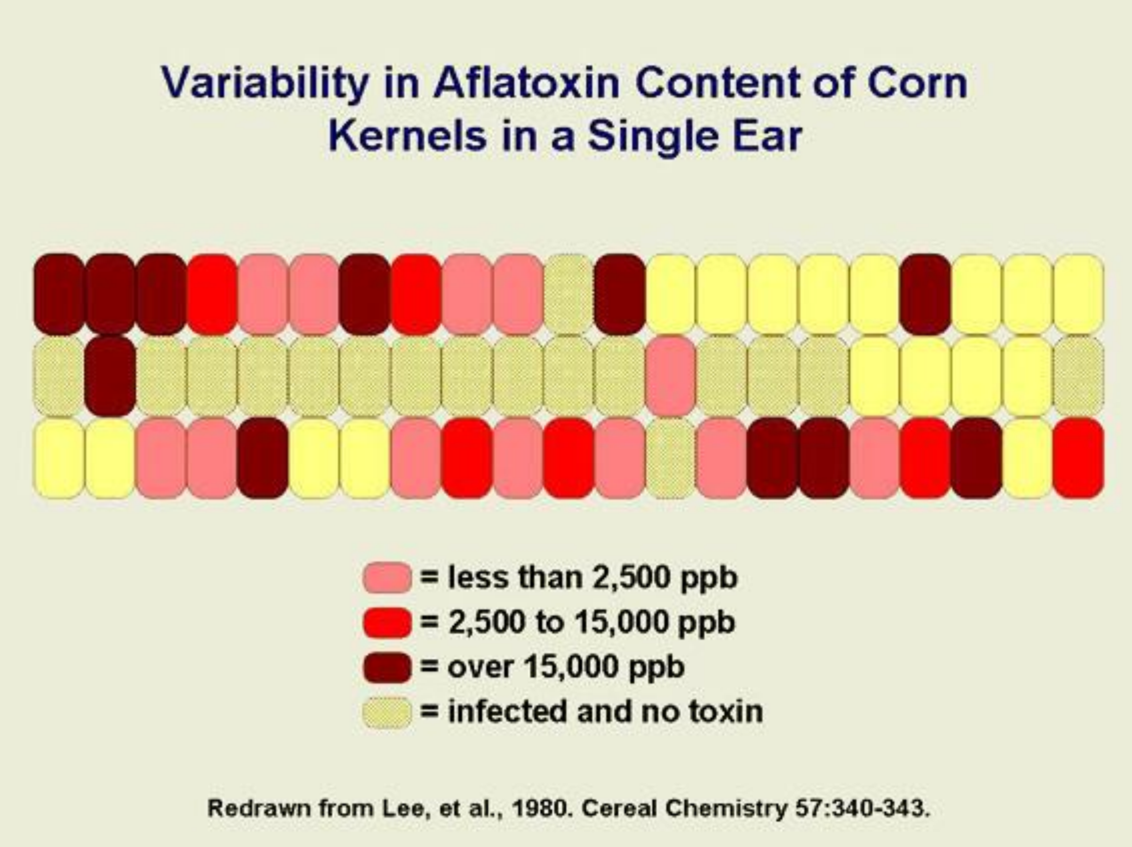
VI. Determining mycotoxin levels

- Levels of disease are not necessarily correlated with mycotoxin contamination
- Mycotoxin levels in a crop are variable within a field, plant, and individual kernels
- Proper sampling is necessary to estimate overall levels
- Many methods for mycotoxin detection and quantification are available

VI. Determining mycotoxin levels

- **Sampling: mycotoxin concentrations within a crop (field, plant, kernel) are highly variable**

Fusarium ear rot



VI. Determining mycotoxin levels

- **Sampling equipment and procedures**

1. Manual Sampling

  - Grain probe or trier (barges, box cars, trucks, hopper containers)
  - Bag trier (sacked grains)
  - Pelican sampler (sampling grain in a falling stream)

2. Pneumatic Sampling or Hydraulic Probes (terminal elevator or processing plant probe)

3. Mechanical Sampling Systems

SOURCE: http://www.romerlabs.com/us/knowledge/sampling-for-mycotoxins/

VI. Determining mycotoxin levels

- **Detection and quantification**
  - At buying point
  - Commercial kits (qualitative, quantitative)
  - Analytical labs (HPLC, GC/MS)
    - Commercial laboratories
    - University testing services

VII. Management strategies

- Good agricultural practices (GAP)
  - Irrigation (avoid drought stress) – not always feasible/affordable
  - Cultural practices – sanitation, tillage, crop rotation, plant and harvest date
- Resistant cultivars
  - Overcome by environment
- Insect control (sprays, Bt crops)
  - Helps but inconsistent

VII. Management strategies - aflatoxin

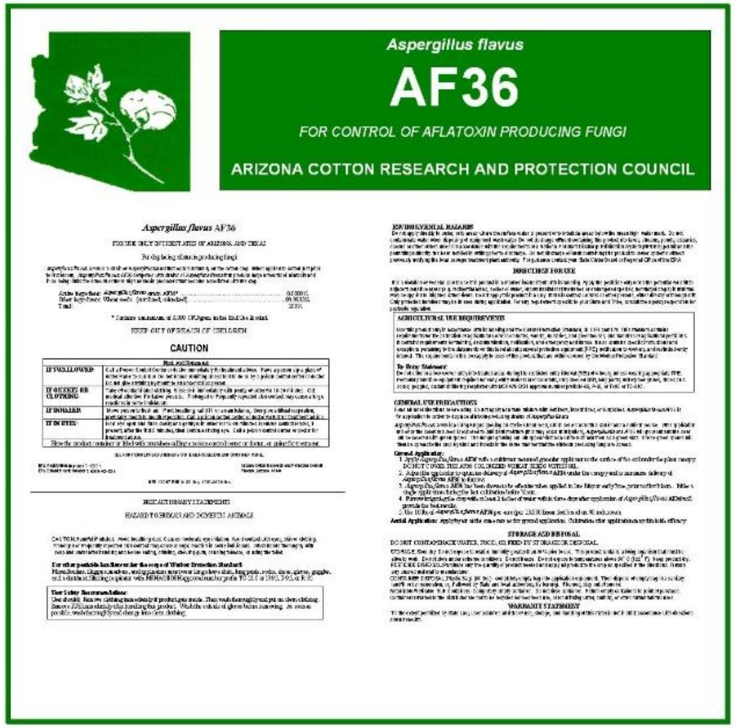
Competitive displacement of aflatoxin-producing fungi. Over the past few decades, an estimated 10^6 acres of crops have been treated with strains of *A. flavus* that do not produce aflatoxins

	Aflatoxin B_1 ($mg\ kg^{-1}$)	Infection (%)	*A. flavus* on crop (spores/g)	Applied strain (%)
Treated	0.3 b	1.03 a	23,949 a	100 a
Control	81.8 a	0.85 a	28,949 a	7 b

Cotty 1994, *Phytopathology*

VII. Management strategies - aflatoxin

- Biopesticides – aflatoxin control



Afla-Guard® GR

VII. Management strategies

- Good agricultural practices
  - Early harvesting
  - Proper harvesting
  - Physical treatment
  - Sanitation
  - Proper storage
  - Insect management
  - Other methods
- Biological control
- Chemical control
- Decontamination
- Breeding for resistance
- Legislation
- Surveillance and awareness creation

VII. Management strategies

- Postharvest
  - Sorting and physical separation of contaminated grain (de-hulling)
  - Proper storage environment (dry, cool)
  - Maintain grain moisture below 15%
  - Control storage pests
  - Detoxification

VII. Management strategies

- Detoxification
  - Blending (aflatoxin) – typically not allowed by FDA
  - Ammoniation (aflatoxin) – not allowed for corn, allowed for cottonseed (with restrictions)
  - Heat deactivation – most mycotoxins are heat stable
  - Microbial degradation
  - Feed additives (binding agents)

Conclusion

- Mycoses are the best-known diseases of fungal etiology
- Mycotoxin (toxic secondary metabolites) describes pharmacologically active mold metabolites characterized by vertebrate toxicity
- Strain-specific
- Elicit overlapping toxigenic activities including carcinogenicity, inhibition of protein synthesis, immunosuppression, dermal irritation, and metabolic perturbations
- Mold contamination does not demonstrate mycotoxin contamination
- In the absence of appropriate investigative criteria and laboratory tests mycotoxicoses will remain diagnostically daunting diseases