# Mycotoxins in Animal Feed: Risks to Animal & Human Health

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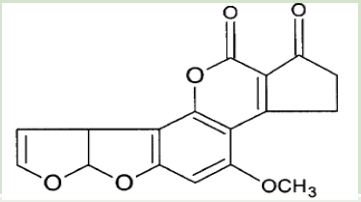
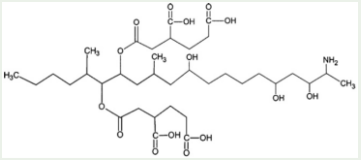
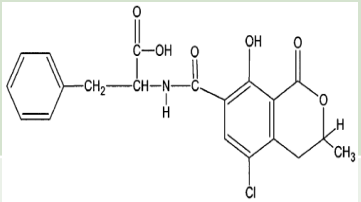
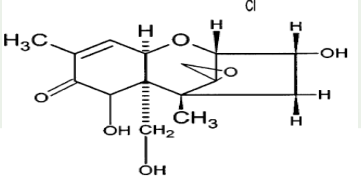
# Presentation outline

- What are mycotoxins?
- Key agricultural mycotoxins in animal feed
- US regulations: mycotoxins in animal feed
- Animal health effects
- Potential human health effects
- What can we do about it?

# Mycotoxins: What are they?

- Toxic & carcinogenic chemicals produced by fungi
- Long history of mycotoxins affecting society
  - Leviticus 14:37
  - 11th c.: *Claviceps purpurea* produces ergot in rye → St. Anthony's Fire
  - Mysterious human & animal deaths in 1930s (Great Depression horses)
  - 1960 aflatoxin discovery: UK turkey deaths
  - Today: several dozen mycotoxins identified

# Major classes of mycotoxins, associated foods & health effects, & species affected

| Mycotoxin | Produced by | Chemical structure | Contaminated products | Animals affected | Clinical effects |
|---|---|---|---|---|---|
| **Aflatoxin** | *Aspergillus flavus; A. parasiticus* |  | Corn, peanuts, cottonseed, tree nuts, dairy products | Swine, dogs, fish, cattle, poultry, humans | Liver lesions, liver cancer, growth impairment |
| **Fumonisin** | *Fusarium* spp |  | Corn, silage | Swine, horses, humans | Pulmonary edema, leukoencephalomalacia (horses), neural tube defects, growth impairment |
| **Ochratoxin** | *Aspergillus, Penicillium* spp |  | Cereals (esp. oats), nuts, coffee, grapes | Swine, humans | Kidney and liver damage, cancer |
| **Deoxynivalenol (vomitoxin)** | *Fusarium* spp |  | Wheat, barley, oats, corn | Swine, cattle, poultry, horses, humans | Feed refusal, anorexia, vomiting, reduced growth |

# US Food & Drug Administration mycotoxin regulations, animal feed

### Aflatoxin (action levels)

| Class of Animal | Action level |
|---|---|
| Finishing beef cattle | 300 ppb |
| Beef cattle, swine or poultry | 300 ppb |
| Finishing swine | 200 ppb |
| Breeding cattle & swine, mature poultry | 100 ppb |
| Dairy animals, pets | 20 ppb |

### Fumonisin (industry guidelines)

| Class of Animal | Industry guideline |
|---|---|
| Swine and Catfish | 10 ppm |
| Breeding Ruminants, Poultry, Mink | 15 ppm |
| Ruminants >3 months; Mink for pelt production | 30 ppm |
| Poultry for Slaughter | 50 ppm |
| Horses | 5 ppm |

### DON (industry guidelines)

| Class of Animal | Industry guideline |
|---|---|
| Ruminating beef and feedlot cattle older than 4 months | 10 ppm |
| Chickens | 10 ppm |
| Swine & all other animals | 5 ppm |
| All other animals | 5 ppm |

# Occurrence of mycotoxins in animal feed

**Worldwide mycotoxin survey in >25,000 finished feed samples: 81% samples contaminated with at least 1 mycotoxin** (Marugesan et al. 2015)

| Parameters | AF | DON | FUM | OTA |
|---|---|---|---|---|
| Percent positive (%) | 40 | 60 | 72 | 36 |
| Average level (µg/kg) | 7 | 280 | 687 | 5 |
| Maximum (µg/kg) | 1,165 | 9,903 | 10,282 | 595 |

**Economic impacts:**

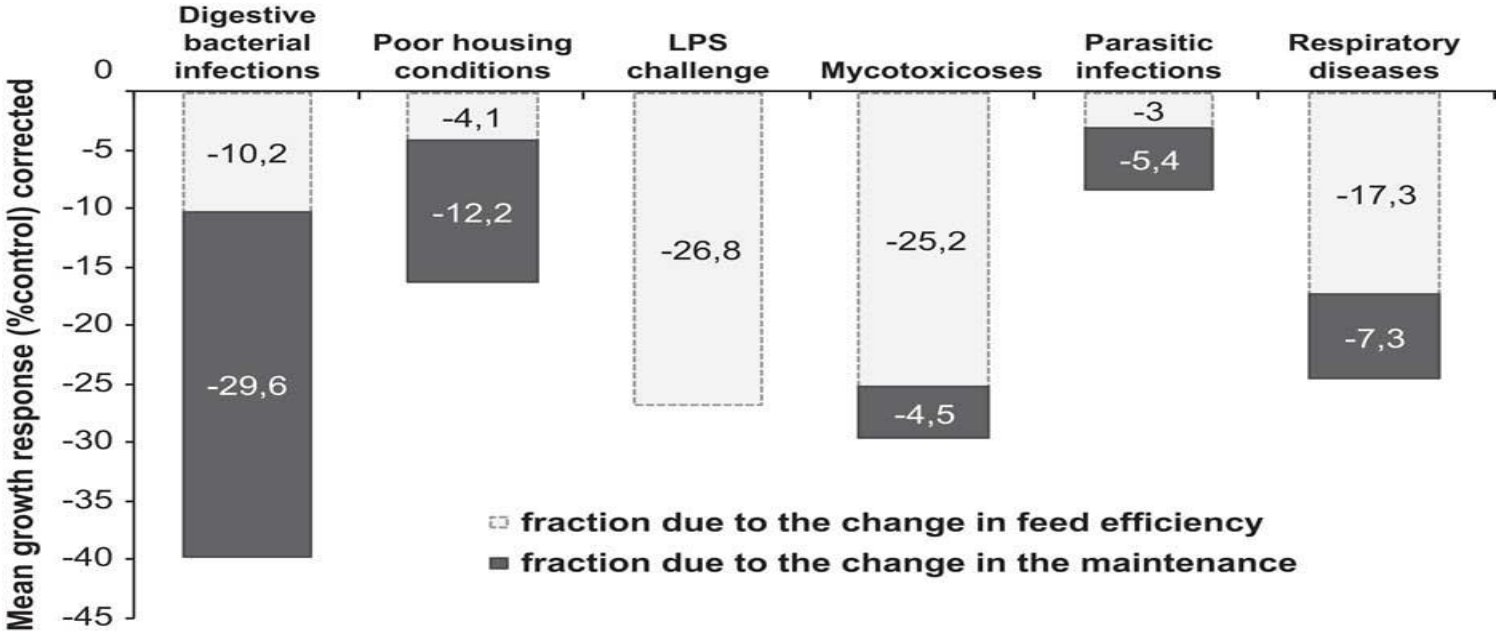
- >$1 billion annual loss in 2017 USD from mycotoxins in US crops (Vardon et al. 2003)
- Economic losses due to effects on livestock productivity and costs of meeting regulatory requirements

**Animal health Impacts:**

- Reduced feed efficiency
- Gastrointestinal dysfunction
- Immune system dysfunction

# Mycotoxins reduce animal feed efficiency

At mycotoxin doses found in real animal feed, mycotoxicoses can cause 30% reduction in growth, 85% of which is attributable to feed inefficiency (meta-analysis of swine data).




*Source: Pastorelli et al. 2012, 6:952–61*

- ***Why might this be happening?***

# Mycotoxins cause gastrointestinal dysfunction (cytokine expression)

- ***Cytokine expression within the intestine of mammals due to exposure to DON and fumonisin [FB] (Bracarense et al. 2012). Aflatoxin has similar effects (Turner et al. 2007).***

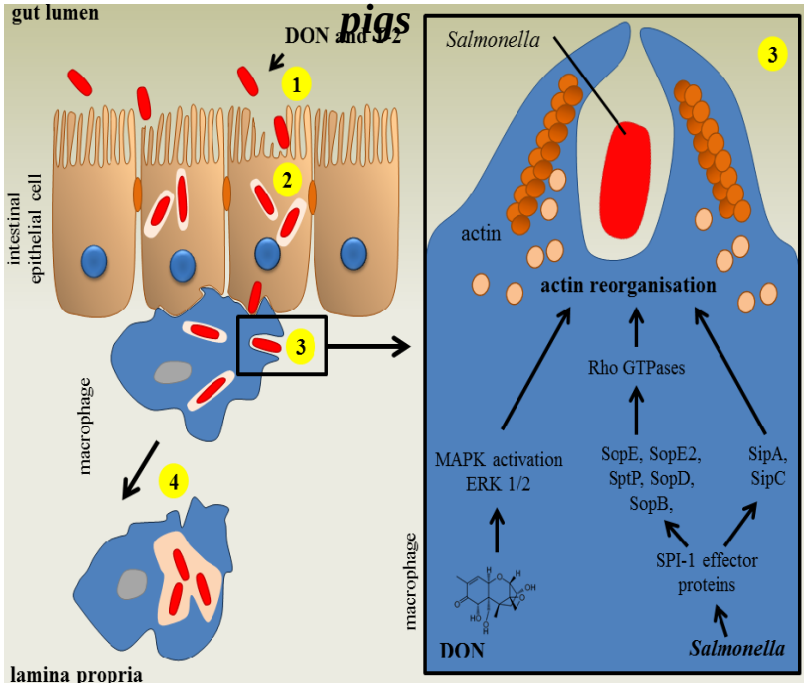
| | Diet treatment | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Control | | DON | | FB | | DON + FB | |
| Cytokine | Mean | SEM | Mean | SEM | Mean | SEM | Mean | SEM |
| Intestinal portion | | | | | | | | |
| Jejunum | | | | | | | | |
| IL-1β | 1·00[a] | 0·17 | 1·78[b] | 0·12 | 1·34[a] | 0·11 | 1·46[a,b] | 0·14 |
| TNF-α | 1·00[a] | 0·08 | 1·29[a] | 0·12 | 0·88[a] | 0·14 | 1·56[a] | 0·33 |
| IL-6 | 1·00[a] | 0·12 | 2·17[b] | 0·30 | 1·14[a] | 0·11 | 1·35[a] | 0·14 |
| IL-8 | 1·00[a] | 0·09 | 1·78[a] | 0·52 | 1·38[a] | 0·40 | 1·02[a] | 0·12 |
| MIP-1β | 1·00[a] | 0·08 | 1·42[b] | 0·14 | 1·36[a,b] | 0·18 | 1·27[a,b] | 0·16 |
| IL-2 | 1·00[a] | 0·16 | 1·80[b] | 0·25 | 1·74[a,b] | 0·31 | 1·56[a,b] | 0·26 |
| IL-12p40 | 1·00[a] | 0·09 | 1·71[b] | 0·26 | 1·36[a,b] | 0·13 | 2·01[b] | 0·49 |
| IFN-γ | 1·00[a] | 0·16 | 1·29[a,b] | 0·08 | 1·43[b] | 0·10 | 1·35[a,b] | 0·17 |
| IL-10 | 1·00[a] | 0·11 | 1·34[a,b] | 0·24 | 1·51[b] | 0·19 | 1·63[b] | 0·17 |
| Ileum | | | | | | | | |
| IL-1β | 1·00[a] | 0·19 | 2·00[b] | 0·19 | 1·73[b] | 0·24 | 1·63[b] | 0·13 |
| TNF-α | 1·00[a] | 0·08 | 1·49[b] | 0·10 | 1·42[b] | 0·11 | 1·71[b] | 0·23 |
| IL-6 | 1·00[a] | 0·20 | 2·13[b] | 0·21 | 1·02[a] | 0·13 | 0·96[a] | 0·24 |
| IL-8 | 1·00[a] | 0·18 | 1·18[a] | 0·08 | 1·48[a] | 0·38 | 1·53[a] | 0·30 |
| MIP-1β | 1·00[a] | 0·06 | 1·50[a] | 0·30 | 1·19[a] | 0·07 | 1·42[a] | 0·22 |
| IL-2 | 1·00[a] | 0·12 | 1·00[a] | 0·22 | 1·25[a] | 0·16 | 1·04[a] | 0·11 |
| IL-12p40 | 1·00[a] | 0·07 | 1·04[a] | 0·11 | 1·09[a] | 0·07 | 1·34[a] | 0·14 |
| IFN-γ | 1·00[a] | 0·12 | 1·43[a] | 0·21 | 1·26[a] | 0·09 | 1·90[a] | 0·48 |
| IL-10 | 1·00[a] | 0·13 | 1·14[a] | 0·12 | 1·23[a] | 0·14 | 1·57[a] | 0·38 |

*Source: Bracarense et al. Br. J. Nutr. 2012, 107:1776–86*

# Mycotoxins change intestinal epithelium, increasing animal susceptibility to infectious diseases

- DON acts as a predisposing factor by damaging the intestinal mucosa, leading to leakage of nutrients into the intestinal lumen
- Broiler chickens fed a diet contaminated with 5 mg DON/kg of feed were found to be more prone to develop necrotic enteritis lesions compared to controls in a normal diet (Antonissen et al. 2014)
- Moreover, swine exposed to aflatoxin in feed experienced **increased** proinflammatory cytokines, but **reduced** vaccine efficacy (Meissonnier et al. 2008)

***The impact of DON and T-2 toxin on a Salmonella Typhimurium infection in pigs***




*Antonissen et al. Toxins. 2014, 6, 430-452*

# If livestock consume mycotoxins, what is **human health** impact?

- Dairy animals that consume aflatoxin B1 secrete **aflatoxin M1 (AFM1)** in milk
- AFM1 has 10% cancer potency of AFB1 (JECFA 2001)
- FDA regulates AFM1 at 0.5 ug/kg allowable in dairy (EU: 0.05 ug/kg)

- **Ochratoxin A** bioaccumulates in animal blood and (to limited extent) swine muscle meat
- OTA risk highest for populations that consume blood sausage, black pudding, other blood products; and to limited extent, pork
- Some kidney toxicity risk

**Occurrence of AFM1 in dairy products globally**

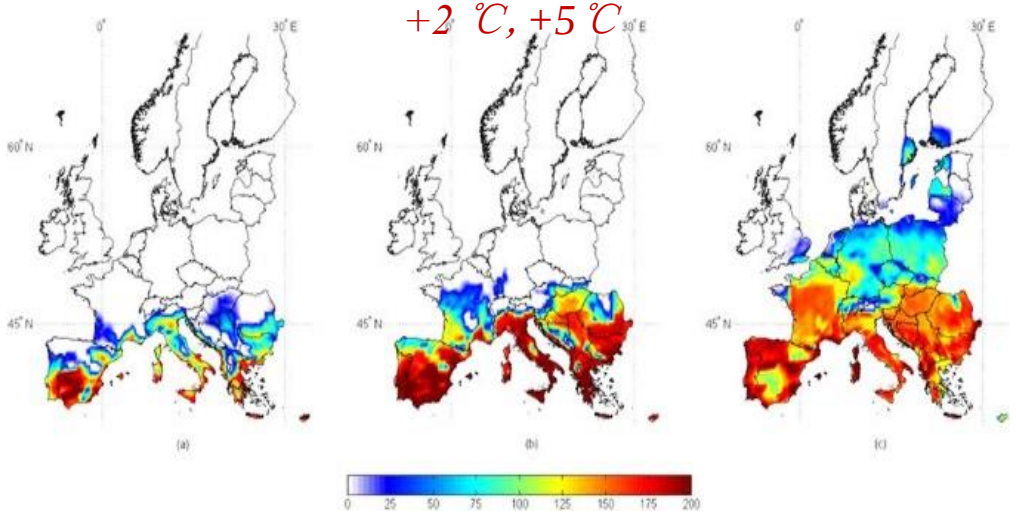
| Country | Sample | % AF-positive samples | Min–Max (µg/kg) |
|---|---|---|---|
| **Kuwait** | White cheese | 80 | 0.024–0.45 |
| **Turkey** | Cheese | 94 | 0.012–0.38 |
| | Yoghurt | 56 | 0.0025–0.078 |
| | Dairy dessert | 52 | 0.0015–0.08 |
| | Butter | 100 | 0.01–7.0 |
| | Cream cheese | 99 | 0–4.1 |
| | Yoghurt | 88 | 0.01–0.48 |
| **Iran** | White cheese | 80 | 0.052–0.75 |
| | Cream cheese | 72 | 0.058–0.79 |
| | Livan cheese | 65 | 0.03–0.31 |
| | Cheese | 53 | 0.082–1.25 |
| | White cheese | 60 | 0.041–0.37 |
| | Feta cheese | 83 | 0.15–2.4 |
| **Libya** | Cheese | 75 | 0.11–0.52 |
| **Brazil** | Cheese | 30 | 0.091–0.3 |
| **Greece** | Feta cheese | 0 | – |
| **Pakistan** | White cheese | 78 | 0.004–0.6 |
| | Cream cheese | 59 | 0.004–0.46 |
| | Butter | 45 | 0.004–0.41 |
| | Yoghurt | 61 | 0.004–0.62 |
| **Serbia** | Milk products | 38 | 0.27–0.95 |

*Becker-Algeri et al. J Food Sci. 2016; 81:R544-52*

# What causes mycotoxin problems in animal feed?

- Climate factors
  - Warmer temperatures favor certain fungi
  - Drought, rainfall
- Environmental factors
  - Insect pests
  - Suitability of hybrid for region
- Crop & livestock grower practices
  - Harvesting when wet, rather than allowing crop to “dry down”
  - Insufficient drying
  - Wet, warm, pest-ridden storage conditions
  - Long periods of animal feed storage

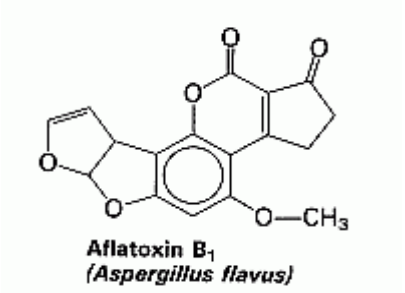
*Risk maps for aflatoxin contamination in maize at harvest in 3 different climate scenarios, present, +2 ℃, +5 ℃*




*Battilani et al. Sci Rep. 2016;6:24328*

# Interventions to reduce mycotoxin risk

- Preharvest
  - Good agricultural practices
  - Genetically enhancing plants' resistance
  - Biocontrol
- Postharvest
  - Improved sorting, drying, food storage



Aflatoxin $B_1$
*(Aspergillus flavus)*

- Dietary
  - Improved dietary variety
  - Dietary enterosorbents (binders)
    - NovaSil used commonly in US animal feed
  - Dietary chemoprevention
    - Chlorophyll, chlorophyllin
    - Compounds in cruciferous & Allium vegetables
    - Triterpenoids (in grasses, herbs, apple peels)

# Summary

- Mycotoxins have posed a danger to human & animal health for millennia
- Mycotoxins occur frequently in animal feed worldwide
- Despite regulations, animals can still suffer adverse health effects
- Interventions exist to reduce the mycotoxin problem