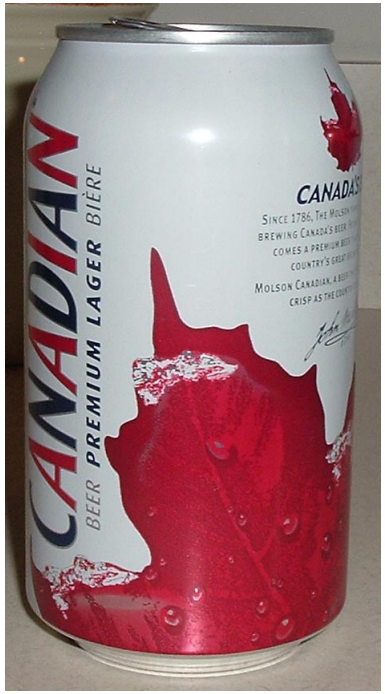
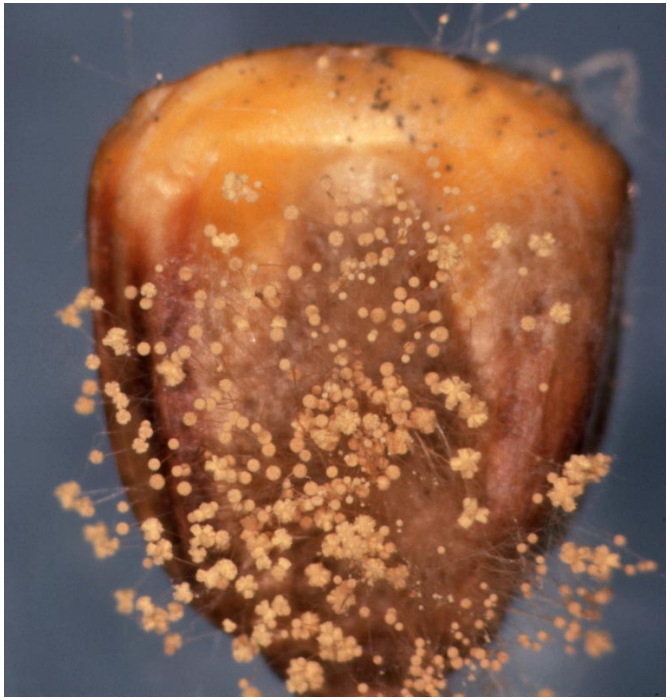
Mycotoxins

What are they?
Where do they occur?
What do they do?
Who makes them?
What is risk to food supply?





Important mycotoxins

Aflatoxins
Ergot alkaloids
Trichothecenes
Zearalenones
Fumonisins
Patulin
Ochratoxin

Mycotoxin producing fungi

Aspergillus - aflatoxin, ochratoxin
Penicillium - ochratoxin, patulin
Fusarium - trichothecenes, zearalenones
Stachybotrys - trichothecenes
Alternaria - alternariol, tenuazonic acid
Claviceps - ergotamine, ergovaline
Trichoderma - trichothecenes
Myrothecium - trichothecenes
Pithomyces - sporidesmin

Ascomycetes: Hypocreales, Eurotiales, Dothideales

Mycotoxicosis: poisoning caused by fungal toxins in foods

Mycotoxins are produced by some of the most common and widespread fungi in the environment. Function, presumed to deter fungivory by mammals, insects or other fungi, or to allow fungi to compete with animals and microbes for the substrate.

Mycosis, mycotic infection: disease caused by fungal infection. Diseases caused by fungal toxins will be dealt with separately from infectious diseases caused by fungi.

Mycotoxin: low molecular weight fungal metabolite capable of causing toxic responses in humans and animals. Chemistry varies.

Mycotoxin effects

- animal growth (weight gain)
- animal products (e.g. eggs, milk, meat)
- reproductive disorders
- mortality

In Humans:

- acute mycotoxicosis
- cancers
- diseases, nutritional disorders

Mycotoxin symptoms

- high concentrations: acute disease, death
  - organs: kidney, liver, stomach, skin, brain, lung
- low concentrations: carcinogenic, mutagenic, teratogenic; nutritional and reproductive disorders.

Mycotoxins in food supply

Estimated that 25% of world's crops are contaminated with mycotoxins. Chronic exposures in populations of some developing countries.

In U.S. most common crops with mycotoxins are:
peanuts, cornmeal, cottonseed, pecans, hay
mycotoxins also may occur in meat, eggs, dairy products

Aflatoxins are monitored in several commodities by USDA
Other mycotoxins are not regulated in the USA but some are regulated by the EU, so some US exports are monitored.

Allowed aflatoxin levels (USA) vary from 300 µg/kg in animal feed to 0.5 µg/kg in milk for human consumption

Mycotoxins are a current, continuing, chronic problem for world food producers

Mycotoxins are monitored by regulatory agencies, but nobody is perfect

Jan 2006

Dog Deaths Surpass 100 Despite Toxic Pet Food Recall

The Food and Drug Administration has reportedly determined that a pet food company improperly tested or failed to test corn shipments for a deadly fungus.

The State newspaper in Columbia, South Carolina, says the FDA found Diamond Pet Foods allowed the tainted corn into a plant and didn't properly test for the naturally occurring poison.

An FDA investigator says the agency started the investigation after the company recalled about one million pounds of dry dog food in December.

The newspaper says the FDA report due out this week doesn't penalize the company.

April 2013

Recalls of Aflatoxin-Contaminated Dog Food Have Begun

Reuters reports high levels of aflatoxins have been discovered in bags of dog food on store shelves in Iowa. And according to Michael Wright, the CEO of Pro-Pet, a pet food company in Ohio that recently learned some of its product was contaminated with aflatoxins, *"Last year's corn crop – it's a huge issue. We test every load coming in. And we reject a lot of loads."*

During the last week of February, the Hy-Vee Inc. grocery chain was forced to recall five different products in its private dog food line due to high levels of aflatoxins in the corn used in the formulas. The dog food was produced at a Kansas City Pro-Pet plant and distributed across eight Midwestern states.

"This year the toxin was much more prevalent. According to crop insurance data from the U.S. Department of Agriculture, payouts for mycotoxins, of which aflatoxin is the most common, totaled nearly $75 million, triple the level of a year ago.

Nearly 85 percent of the claims were filed in six states: Arkansas, Illinois, Indiana, Kansas, Mississippi and Missouri."

Reuters Feb 2013

Dog Food Recall

River Run and Marksman recalled products

Aflatoxin Information

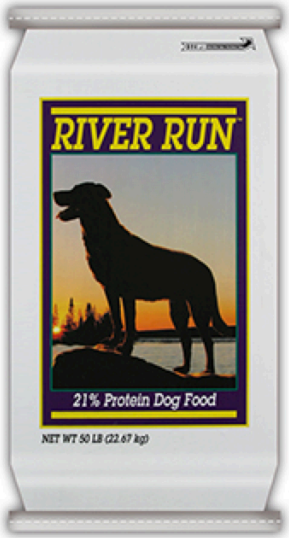
FAQ

River Run and Marksman Dog Food: Recalled Product List

Share this:

Recall Dates: Dec. 1, 2010 through Dec. 1, 2011

Cargill has announced a voluntary recall of the following products in 13 states and 2 territories: Kansas, Missouri, Northeast Oklahoma, Arkansas, Louisiana, Mississippi, Tennessee, Western Kentucky, Southeast Indiana, Southern Illinois, Hawaii, and limited areas of Florida, California Guam, and the Virgin Islands. The products may contain higher-than-acceptable levels of aflatoxin, a substance found widely in nature as a result of



YORKTON THIS WEEK

Mycotoxins in fall and winter feed supply

October 22, 2014

More and more cattle producers are using fall and winter grazing to extend the grazing season, and for good reason. This management practice is a cost-effective option that reduces labour requirements and can keep livestock out of the corrals until just before calving season. Maximizing forage yield while maintaining forage quality is the goal for most producers. However, one area that is commonly overlooked is that of plant disease and the effects that mycotoxins can have on grazing livestock.

Crop disease is largely dependent on the weather conditions and for that reason it is very hard to manage. Cool and moist conditions when cereal crops were flowering has resulted in an increase of crop disease, particularly fusarium and ergot. Mycotoxins can be quite harmful to livestock, and while ruminants are generally more tolerant to mycotoxins than other livestock species, they are still at risk.

An elevated level of the mycotoxin, ochratoxin A, was detected in one batch of Girolomoni pasta. The batch is being recalled and point of sale notices are being displayed in the shops supplied. Consumers are advised not to eat the implicated pasta.

Friday, 10 October 2014

Eliminating Aflatoxin Goal Of Kenya Program

Jeff Caldwell
10/06/2014 @ 9:34am
Multimedia Editor for Agriculture.com and Successful Farming magazine.

Aflatoxin is a problem in some corn fields in the U.S., where infection of the fungus typically means either additional storage costs or occasional refusal of loads of the grain at the local elevator.

In Kenya, though, the crop disease means a lot more. Corn is grown more for human consumption there, and aflatoxin can cause serious illness and death if enough is consumed. The U.S. Centers for Disease Control (CDC) considers aflatoxin a "public health problem" in Kenya and when the disease started causing broader-scale health problems and fatalities about a decade ago, officials there said finding and constructing "culturally appropriate storage methods for dry maize" would be of utmost importance in stemming the disease and saving lives.

Mycotoxin contamination of food/grain

May develop/increase during storage but not necessarily caused by storage

Mycotoxins naturally occurring in various grain crops, develop during crop ripening

Not necessarily associated with visible mold

Major mycotoxin groups in food products

Mycotoxin	Products affected	Animals affected	Effects
Aflatoxins	Corn, peanuts, cottonseed, tree nuts, dairy products	Swine, dogs, cats, cattle, sheep, birds, humans	Liver damage, intestinal bleeding, cancer
Ergot alkaloids	Rye, sorghum, pasture grasses	Cattle, sheep, humans	Hallucinations, gangrene, loss of limbs, hastening of birth
Fumonisins	Corn, silage	Horses, swine, humans	Pulmonary edema, leukoencephalomalacia, esophageal cancer, neural tube defects, liver damage
Ochratoxins	Cereal grains, coffee, grapes	Swine, humans	Kidney and liver damage, cancer
Trichothecenes	Wheat, barley, oats, corn	Swine, dairy cattle, poultry, horses, humans	Feed refusal, diarrhea, vomiting, skin disorders, reduced growth
Zearalenones	Corn, hay	Swine, dairy cattle	Enlargement of uterus, abortion, reproductive issues

Ergotism, ergot alkaloids, *Claviceps purpurea*

The Beggars, Pieter Brueghel (the elder), 1568

Ergot alkaloids

Clavine alkaloids
Ergotamine, ergovaline
indole alkaloids, e.g LSD
peptide alkaloids

August 1951, Pont St Esprit, France
mass food poisoning linked to a single bakery
burning, chills, violent pain, hallucinations, seizures, convulsions, due to grain contaminated by *Claviceps purpurea*

Ergotism
poisoning due to *C. purpurea*, "ergot"
numerous historic accounts thought to be related to ergotism
gangrenous ergotism, convulsive ergotism

1929

REPORT ON AN OUTBREAK OF ALLEGED ERGOT POISONING BY RYE BREAD IN MANCHESTER.

By M. T. MORGAN, M.C., M.D.

(*Medical Officer of the Ministry of Health.*)

Ashby and Robertson have recently given an account of an outbreak of illness in Manchester which had come under their notice and which they attributed to the consumption of rye bread made from rye meal contaminated with ergot.

Nature of the illness.

On reference to Robertson's and Ashby's article it appears that the first symptoms observed in the patients (all of whom were Jews) were coldness and numbness in the extremities; tailors, button-makers, etc., noticed their fingers felt numb and they experienced difficulty in keeping up with their work. Sensation was also impaired; they could prick their fingers without feeling anything. Formication was a very typical symptom in all well-defined cases, and many of the patients stated that they experienced a sensation as if an insect was creeping over or under their skin. Itching was also a common symptom. Nervousness, depression, headaches and abdominal pains were frequent, and in the more severe cases ataxia with a staggering gait occurred. In most cases of long standing, the blood pressure was definitely raised, for example, a woman aged 44 had a systolic blood pressure of 174 mm.

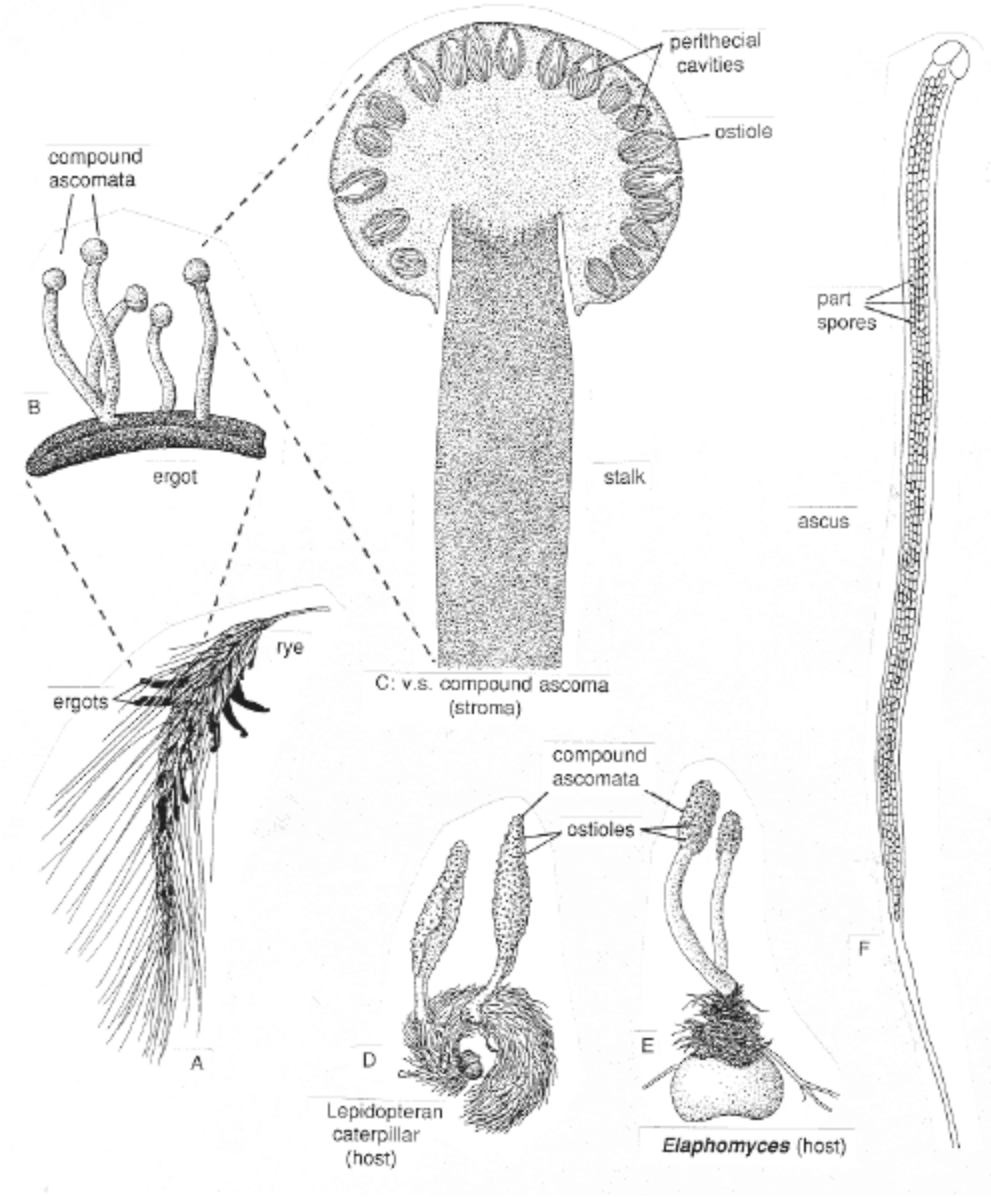
Sclerotia of *Claviceps purpurea*

Sclerotia spur-like, ergot Fr. for spur

Affects major grain crops: rye, wheat, barley, oats

Contain several alkaloid mycotoxins, probably as a deterrent to herbivory by rodents. Sclerotia easily contaminate grain at harvest, alkaloids contaminate flour produced from contaminated grain

Sclerotia germinate to produce a stroma



C. purpurea alkaloids

Symptoms of ergotism: gangrenous form, convulsive form

Ergotamine, vasoconstrictor, can limit blood circulation to digits, limbs. Gangrenous ergotism results. Blood starved limbs begin to decay and eventually drop off.

Sensation of intense heat, "St. Anthony's fire"

Cases of gangrenous ergotism reported in late 1970s in Africa and India

Ergonovine, a second alkaloid in ergot, causes spontaneous abortions in humans and livestock that consume contaminated grain

C. purpurea alkaloids

Ergine, lysergic acid hydroxyethylamide (LSD)

Cause of "convulsive ergotism": tremors, hallucination, sensation of ants crawling on skin (formication), seizures.

Much documented evidence of ergotism in central Europe during the middle ages, consumption of ergotized grain more prevalent among the poor.

Germany 857: "A great plague of swollen blisters…limbs were loosened and fell off before death."

France 944: "A plague of invisible fire…cutting off limbs from the body…the stench of rotten flesh…"

Epidemics of ergotism from 800 – 1800 were preceded by weather conducive to infection of plants by *C. purpurea*, cool, moist spring caused prolonged flowering and increased infections. If harsh winter followed, grains supplies would be depleted and lead to use of contaminated grain.

Witchcraft associated with people suffering from ergotism. Accused witches in the Salem trials of 1692 exhibited classic symptoms of convulsive ergotism. Also contemporaneous symptoms in livestock. Geographic distribution of witchcraft trials in Europe 1500 – 1700 occurred in places where rye was a major food source and where conditions were favorable for *C. purpurea*.

Pharmaceutical uses of ergot alkaloids

Extracts from boiled sclerotia administered to induce labor 1750-1950. Also administered postdelivery to reduce hemorrhaging.

Ergotamine used to treat migraine and cluster headache

LSD psychoactive drug discovered in 1933 by A. Hoffmann

amide derivative of ergot alkaloid lysergic acid

Investigated for potential therapeutic potential

Also for potential “mind control agent” by CIA and chemical warfare agent

The rest is history!

Epichloe typhina (“endophyte”) is a related fungus that causes “choke disease” of grasses. Infected grass plants contain various alkaloids that are supressive to insect herbivores, also to mammalian herbivores.

symptoms of endophyte toxicosis

An endophyte living inside tall fescue, a popular forage crop, can be toxic to livestock. Fescue toxicosis causes rough hair coats, poor body temperature regulation and lower rates of gain in cattle and reproduction problems in horses.

“sleepy grass” (sw USA) and “dunken horse grass” (China) named for their narcotic effects on grazing animals, caused by fungal endophytes

sod webworm

bluegrass billbug

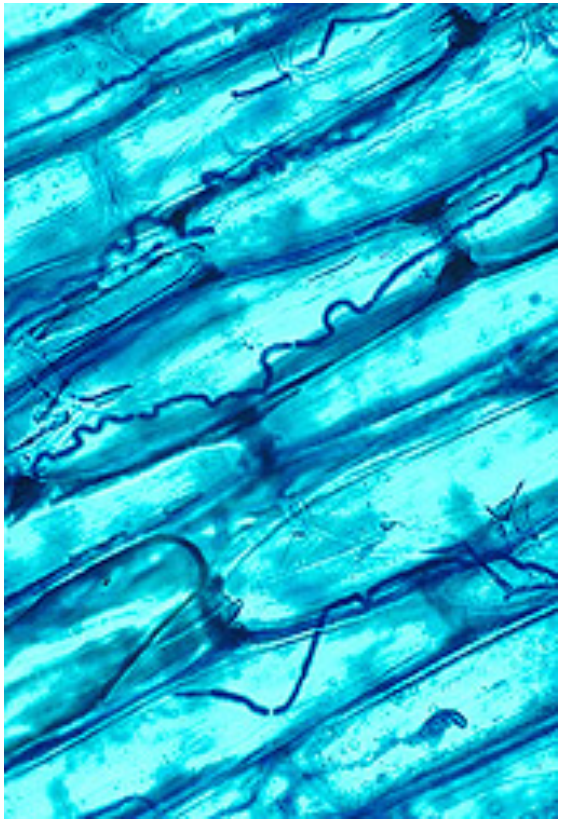
Inhibition of herbivory by pests makes endophyte infected grass preferred for lawns and golf courses

Effects of endophyte alkaloids on mammals:

- elevated body temperature
- reduced feeding
- reduced fertility
- reduced lactation
- spontaneous abortion
- vasoconstriction
- gangrene
- tremors (ryegrass staggers)
- death

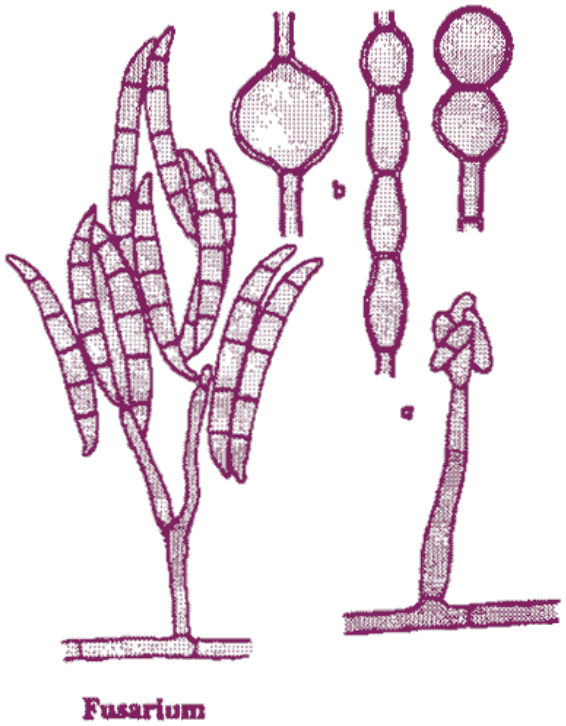
Benefits to grass host

- insect feeding deterrence
- drought resistance
- vigor
- disease resistance



Mycotoxins produced by *Fusarium*

Fusarium wheat scab F. graminearum



Mycotoxins produced by Fusarium species

Trichothecenes

150 structurally related compounds

Fusarium, Trichoderma, Stachybotrys, Cephalosporium,

Primary human food source: *Fusarium graminearum*

deoxynivalenol (DON, vomitoxin)

T-2 toxin

nivalenol

Fumonisins

Fusarium verticilloides (*F. moniliforme*)

equine leucoencephalomalacia

esophageal cancer

Zearelenones

Fusarium graminearum

Estrogen-mimic

Swine estrogenic syndrome

Trichothecenes and Fumonisins

Alimentary toxic aleukia, T-2 toxin

1932, 1944 central Asia, Russia, Kazakhstan

Skin rash, severe GI irritation, often fatal

Symptoms similar to viral hemorrhagic fevers (ebola)

but not contagious

Multiple subcutaneous hemorrhage, bleeding nose and throat

Inflamed throat causes death by strangulation

Correlated with consumption of grain (wheat, millet) left in fields over winter and consumed in spring

Fusarium sporotrichoides, F. poae, F. tricinctum

disease reproduced by feeding infected grain to animals

T-2 toxin effects

Found in corn, wheat, barley, oats, rice, millet, rye
Inhibits protein synthesis
Inhibits DNA/RNA synthesis
Affects actively dividing cells such as GI tract lining
Immunosuppressive

Not regulated by FDA or EU

Vomitoxin, Deoxynivalenol DON

Akakabi-byo (red mold disease)

1933, 1950 - 1970 Japan

Disease associated with grains (wheat, barley) contaminated by red mold

Severe GI irritation, vomiting, hemorrage, headache, hallucinations. Rarely fatal.

"drunken bread" made with contaminated grain

F. graminearum, F. kyushuense implicated

several toxins, deoxynivanol (DON), nivalenol

DON is heat stable, survives cooking

Found in Canadian barley and malt

brewers use 0.5 ppm as general threshold, but may use up to 2-5 ppm

Also found in dry dog and cat food

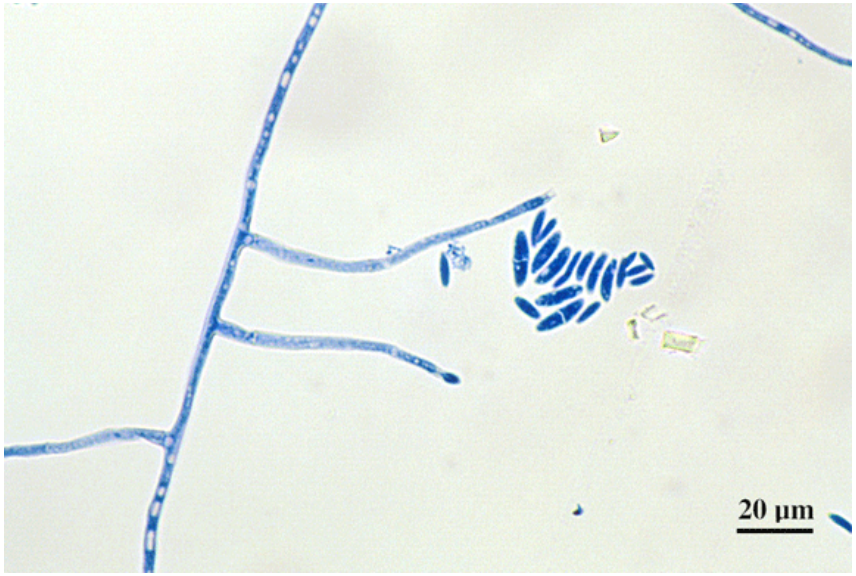
Swine feed refusal

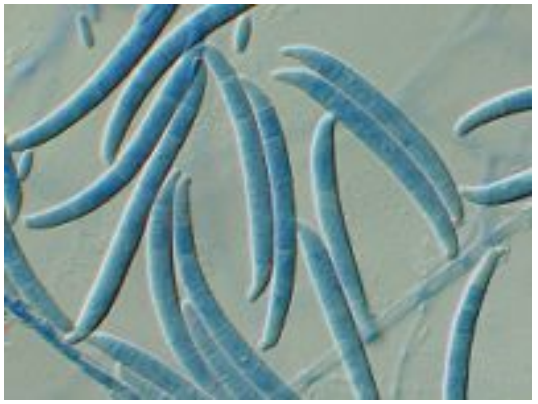
1928,1972 Central USA. Linked to *F. graminearum* contaminated grain (barley)

1965, 1972 weather caused severe maize ear rot contaminated maize used for swine feed

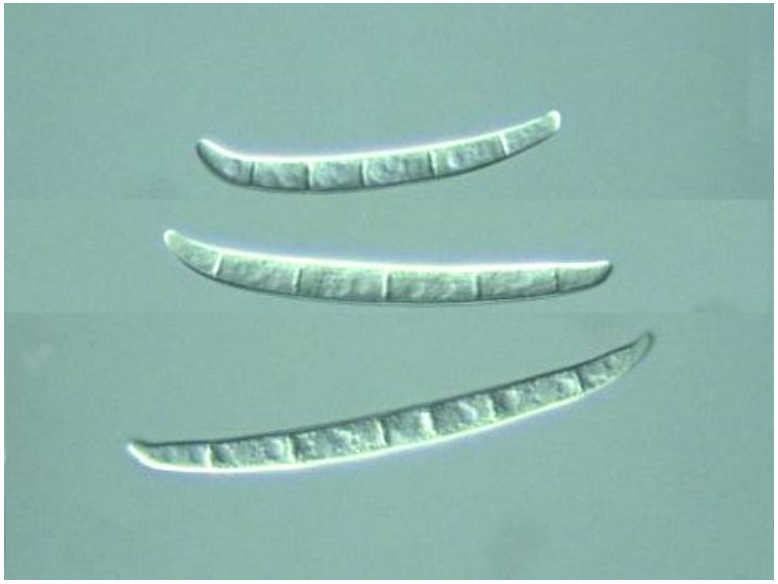
Swine vomited, refused feed, weight loss

Deoxynivalenol (DON), vomitoxin





Fusarium graminearum



Yellow rain

During Vietnam war, symptoms of chemical poisoning in Vietnam, Cambodia, Laos

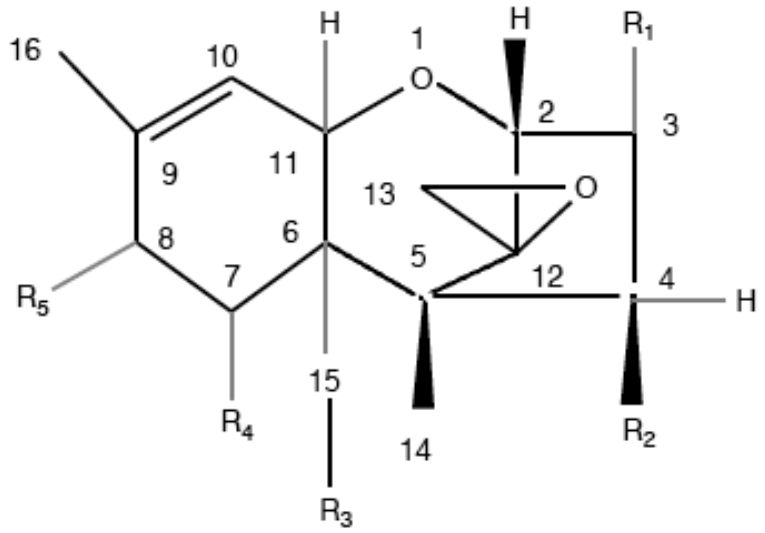
- Chemical warfare of natural contamination?
- Controversial: evidence for both

1981 Secreatary of State Alexander Haig alleged that the Soviet Union and its allies were using chemical weapons in Laos, Kampuchea, Afghanistan. Claimed mycotoxins found in samples smuggled out.

Trichothecenes are highly stable, toxic at low doses and ideal for weaponization

T-2 toxin, DON, nivalenol found in samples and also in blood and urine of victims, but:

- Fusarium spp rare in SE Asia, natural source not known
- Low amounts of mycotoxins found in environmental samples
- Yellow spots contained various types of pollen from local plants and were deposited by cleansing flights of Asian honeybees
- No cases of toxic ‘rain’ reported since 1980s



Generalized structure of the trichothecene ring, with epoxide at C 12

Toxicity due to inhibition of protein synthesis, bind directly to ribosomes

SPECIFIC SIDE GROUPS OF THE MOST ABUNDANT TRICHOTHECENE MYCOTOXINS

Trichothecene	R_1	R_2	R_3	R_4	R_5
T-2 Toxin	–OH	$-OCOCH_3$	$-OCOCH_3$	–H	$-OCOCH_2CH(CH_3)_2$
HT-2 Toxin	–OH	–OH	$-OCOCH_3$	–H	$-OCOCH_2CH(CH_3)_2$
4,15-Diacetoxyscripenol (DAS, also called anguidine)	–OH	$-OCOCH_3$	$-OCOCH_3$	–H	–H
Nivalenol	–OH	–OH	–OH	–OH	=O
Deoxynivalenol (DON)	–OH	–H	–OH	–OH	=O
Macrocyclics	–H	–O–R′–O–		–H	–H

R′: Macrocyclic ester or ester–ether bridge between carbons 4 and 15. The most abundant macrocyclic trichothecenes are verrucarins, roridins, and satratoxin H. Source for this statement: Jarvis BB. Macrocyclic trichothecenes. In: Sharma RP, Salunkhe DK, eds. *Mycotoxins and Phytoalexins*. Boca Raton, Fla: CRC Press; 1991: 361–421.

Occurrence of trichothecenes in food

DON can contaminate barley and malt, and survive the brewing process
1 ug per kg body weight considered the max tolerable daily intake
- 70kg person consume 3.4L of beer with 0.05 mg/ml
- 1994 survey of Canadian beer > 1 ug/L in over 50% of samples

Trichothecene mycotoxins occur in cereal grains worldwide.
- wheat, barley, sorhum, millet
- DON most common trichothecene worldwide
- T-2 toxin, nivalenol more common in Europe than NA

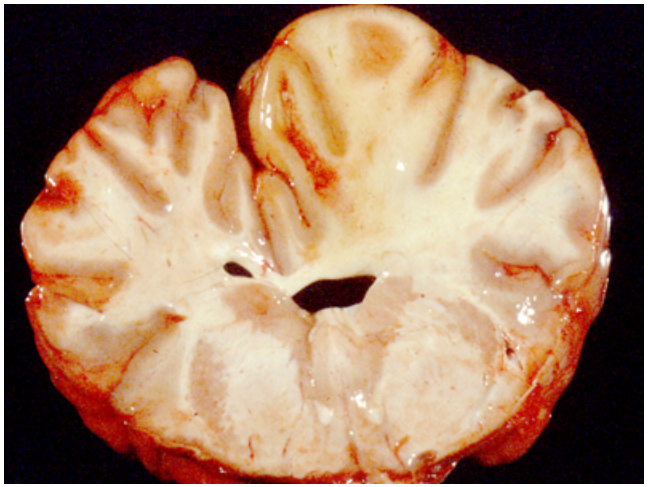
FDA advisory levels for DON:
- 1 ppm (1 mg/L) in finished products for human consumption
- 5 ppm for swine feed, <20% of diet
- 10 ppm for cattle, chicken, < 50% of diet

Fumonisins, *Fusarium verticilloides* (*moniliforme*)

Equine leucoencephalomalacia, “hole in the head”

1900 USA, disease associated with moldy grain (corn, maize)
horses particularly affected, liquified brain matter
Fusarium verticilloides (moniliforme) implicated (1904)
1981 disease reproduced by feeding F. verticilliodes
1989 fumonisin B1 characterized, shown to reproduce symptoms

consumption of contaminated feed causes liquification of the brain in horses



Swine pulmonary edema

1989 USA, hot dry summer, epidemic death of hogs
fluid in lungs
associated with feed of maize “screenings”, low grade grain
disease reproduced by feeding fumonisin B1

Esophageal cancer clusters

1955-1990, Transkei region of S Africa

maize consumption by poor, rural population

epidemiological evidence links consumption of *F. verticilliodes* contaminated maize

Higher incidence of contamination correlated with greater incidence of esophageal cancer

Evidence circumstantial at this point

Neural tube defects

1989 Texas-Mexico border region, Rio Grande valley

hot summer, high fumonisin levels in maize

also concurrent unusually high incidence of equine leucoencephalomalacia

High incidence of neural tube defects in infants, folic acid deficiency, cluster in Mexican-Americans, maize diet

fumonisins block folate uptake

Fumonisin metabolism and effects

Interferes with sphingolipid metabolism
Interferes with folate (vitamin B9) uptake
Accumulate in kidney and liver tissue
Different effects in different animals (e.g. equine leucoencephaly in horses, pulmonary edema in swine)
Carcinogenic (liver), esophageal cancer in humans (?)
Neural tube defects in humans (?)

Fumonisins are only produced by Fusarium species
F. verticillioides, very common and abundant in maize

FDA has 'guidelines':
2 ppm in cornmeal, 3 ppm in popcorn

Zearalenones, Fusarium graminearum

Swine estrogenic syndrome

1950-1960 USA central states

moldy grain used as feed for swine

vomiting, feed refusal (DON), also reproductive system disorder in females

enlarged mammary glands, atrophy of ovaries, infertility, reduced litters, reduced weight

Also in males enlarged mammary, atrophy of testes

symptoms reproduced in mice fed F. graminearum

Zearalenone identified as an estrogenic substance in contaminated maize

Since reported in S. Africa, Europe, N. America, S. America

cattle, swine affected

contaminated barley and malt, survives brewing