

Third Mexican Conference of Graduate Students and Researchers in Canada CEIMEXCAN

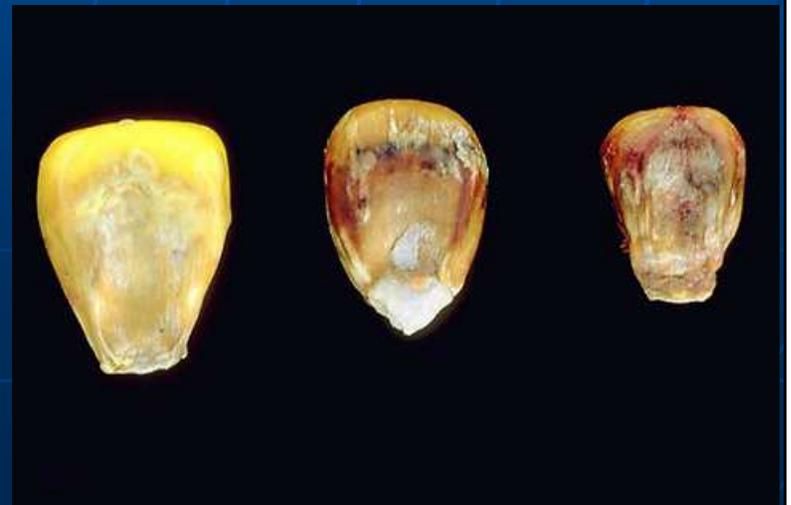
*Fumonisin in corn and the occurrence of
neural tube defects along the Texas–
Mexico border*

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Montreal, October 2008

What are mycotoxins?

- Mycotoxins are natural toxins produced by fungi
- Mycotoxin-producing fungal species are extremely common
- Some mycotoxins provoke serious diseases in humans and animals
- Toxins occur, with varying severity, in agricultural products
- Mexico is a big crops producer, the importance of the presence of these toxins is high
- Mexican regulation establishes limits only for aflatoxins in cereals and cereal products
- No limits are set for other mycotoxins



Fumonisin

- Fumonisin are mycotoxins produced by strains of *Fusarium moniliforme* and *F. proliferatum* commonly associated with corn and other cereal grains
- Only fumonisin B1 and fumonisin B2 have been reported to occur naturally in significant levels in corn and corn-based products
- Mexico has one of the highest rates of human consumption of corn in the world (120 kg per capita per year)
- Total production is about 10.2 million tons for human consumption and 5 million tons for animal feed and other industries



Fumonisin

- FB1 has been shown to cause some animal diseases associated with *Fusarium verticillioides* contaminated feeds such as leukoencephalomalacia in horses, pulmonary edema syndrome in pigs, and hepatocellular carcinoma in rats
- In 2003 the International Agency for Research on Cancer classified FB1 as a Group 2B carcinogen (possible human carcinogen)



F. verticillioides



Ear rot with insect damage

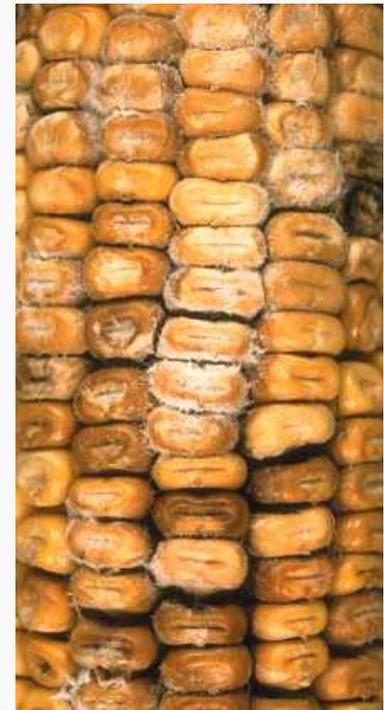


Gibberella stalk rot



root & stalk rot

kernel rot



Fusarium toxins

Species

**Temperature Needed
for Growth**

Factors Affecting Growth

F. graminearum
Gibberella Ear Rot

26-28 °C

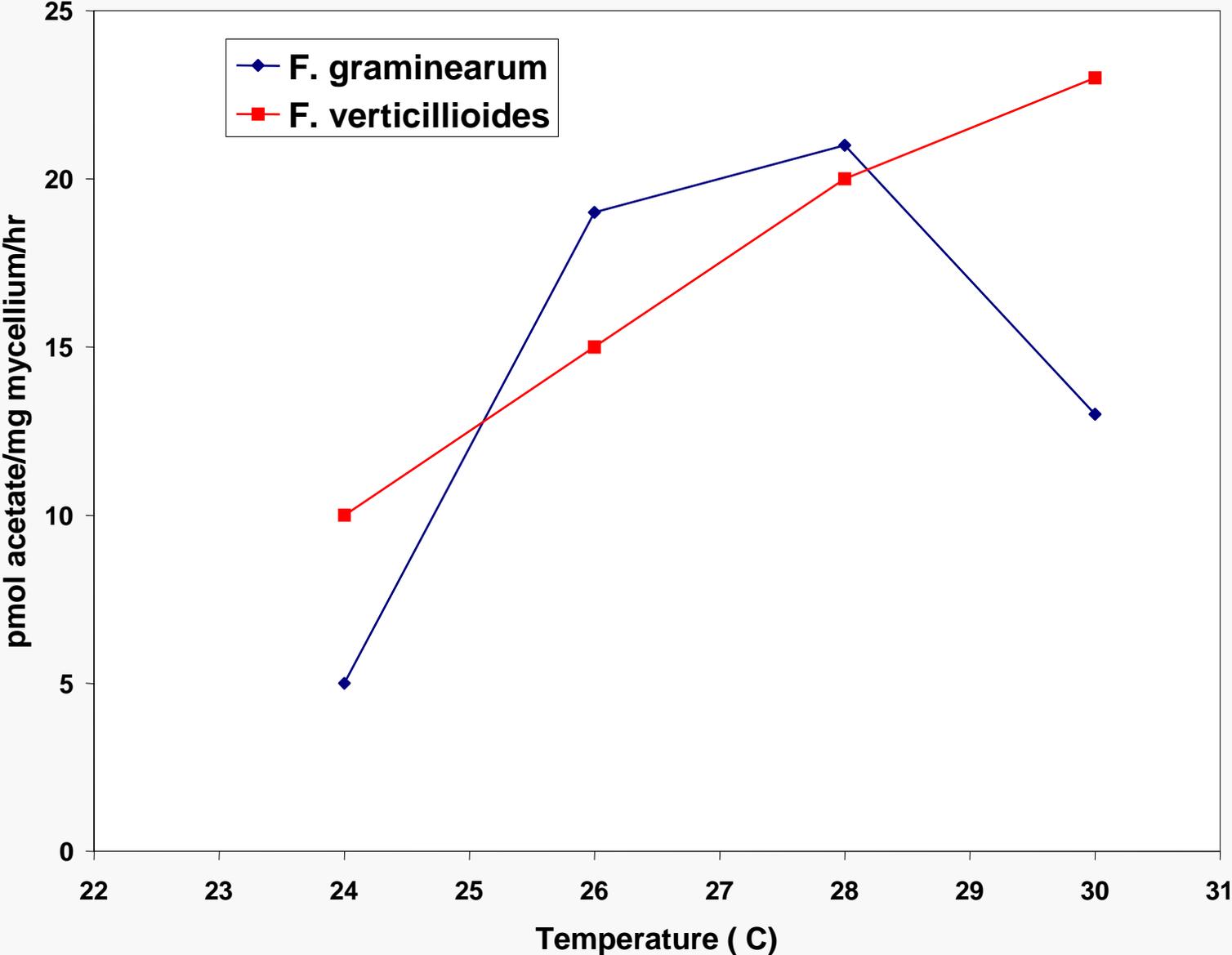
**Needs rain at silking and
during disease progression**

F. verticillioides
Fusarium Ear Rot

> 28 °C

**Drought
Insect stress
Hybrids growing outside
areas of adaptation**

Figure 1. *In vivo* growth rates of *F. verticillioides* and *F. graminearum* in relation to temperature.



Neural Tube Defects

- Along the Texas–Mexico border, the prevalence of neural tube defects among Mexican-American women doubled during 1990–1991
- NTDs are embryonic defects of the brain and spinal cord resulting from failure of the neural tube to close
- Spina bifida and anencephaly are the most severe forms of NTD and cleft palate is most common
- Just before the NTD outbreak, in the fall of 1989, an outbreak of equine leukoencephalomalacia (ELEM) (liquefaction of the white matter of the brain in horses) occurred in the USA
- It was particularly severe in Texas, where, in contrast to the usual one to five ELEM clusters reported, > 40 clusters were reported in < 2 months

Traditional Masa and Tortilla Production Methods

- The presence and recovery of fumonisins in processed foods are affected by the milling and cooking of corn as well as other ingredients present in the recipes
- Nixtamalization is a process by which corn is boiled in a lime solution to produce masa for tortillas
- Four small tortilla plants were visited in Cameron County, Texas, where observations were made on their production methods
- Samples of liquids and solids were collected at each stage of the nixtamalization process, and the pH was recorded
- Samples were analyzed for fumonisin B1

Traditional Masa and Tortilla Production Methods

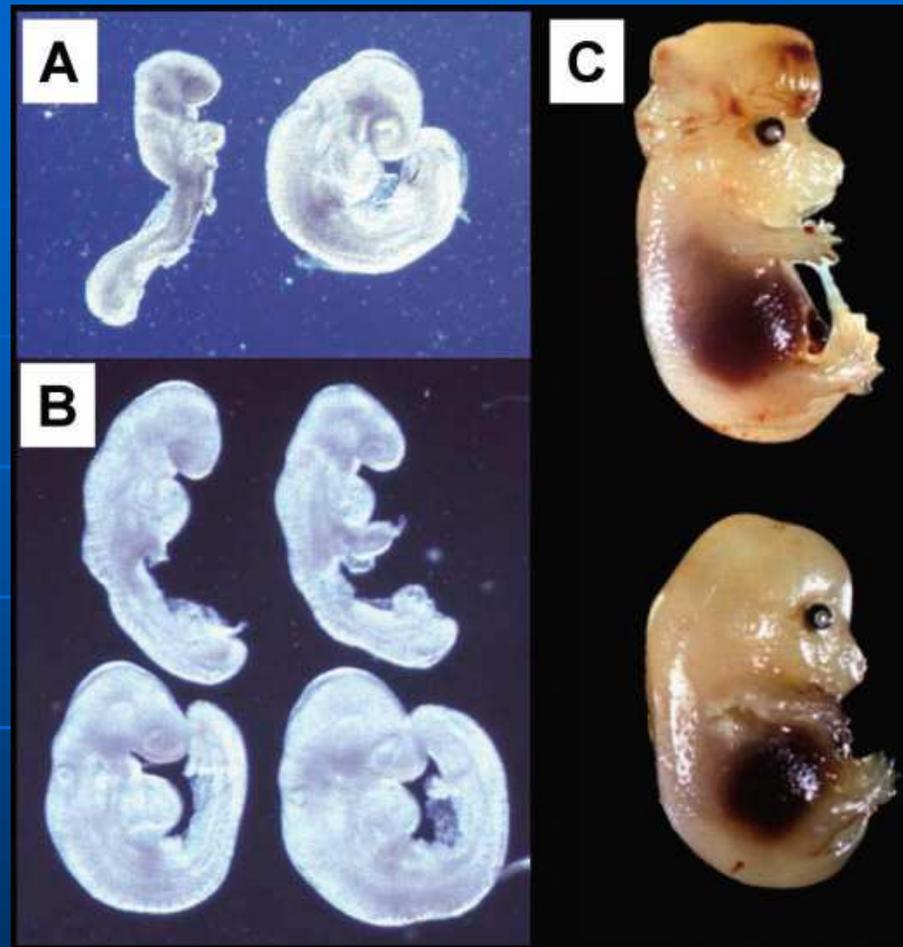
- It was found that production methods were highly variable among the producers visited, with major differences particularly in the amount of lime added and boiling times
- Five initial concentrations of FB1 were tested using irradiated corn kernels inoculated with *F. verticillioides* as the source of FB1
- The amount of FB1 detected in the masa and tortillas decreased as the concentration of $\text{Ca}(\text{OH})_2$ increased, and boiling time had no apparent effect
- Unexpectedly, as the initial concentrations were increased in the corn prior to nixtamalization, greater percentage reductions in FB1 were observed

Traditional Masa and Tortilla Production Methods

- A difference in risk effect was observed between manufactured tortillas and homemade tortillas
- The variations in small-scale tortilla preparation, especially the corn-to-lime ratio, results in wide variations in residual fumonisins
- If tortillas made at home have a consistently lower concentration of lime or poorer quality corn is used, this could potentially explain some of the increased effect seen in homemade tortillas

Neural Tube Defects along the Texas–Mexico Border

- Human outbreak in Texas began during the same crop year as fumonisin levels were very high
- Exposure to fumonisins may play a role in birth defects due to interference with cellular folate uptake
- Because Mexican-Americans in Texas consume large quantities of corn, primarily in the form of tortillas, they may be exposed to high levels of fumonisins at different times
- Findings suggest that fumonisin exposure increases the risk of NTD, proportionate to dose, up to a threshold level, at which point fetal death may be more likely to occur



Effects of fumonisin B1 (FB1) in mouse embryonic development. A: Embryos after 24 h in culture medium containing none (right) or 50 mol/L FB1 (left); B: Embryos after 24 h in medium containing 50 mol/L FB1 (*top*) or 50 mol/L FB1 plus 1 mol/L folic acid (*bottom*) (*panel B* is reproduced from Fig. 3 of Ref. 62). C: Fetus from pregnant LMBC dam injected i.p. with 20 mg/kg body weight FB1 on gestational d 7.5 and 8.5 and killed on d 17.5 (*top*) versus normal fetus at this gestational age (*bottom*).

Marasas et al. 2004.

Conclusions

- The discovery of an association between fumonisin exposure and NTDs may help to clarify the unexplained NTD outbreaks and the increased background prevalence observed in some populations
- In 2001, the FDA recommended that an evaluation of the dietary intake of corn products by specific population groups (e.g., Texas Hispanics) and the levels of fumonisins found in those corn products was needed to fully assess the potential health risks
- Future epidemiologic studies should focus on measuring individual fumonisin intake in specific high-risk populations and assessing its impact not only on the developing embryo but also on other outcomes such as impaired fecundity or pregnancy loss