Aflatoxin Impacts on child growth

Ahmed Kablan, PharmD, PhD.
International Nutrition and Public Health Adviser
Office of Agricultural Research and Policy
Bureau for Food Security (BFS/ARP);
USDA/ARS/Office of International Research Program

akablan@usaid.gov

Substitute Presenter:
William Appaw
Mycotoxin and Food Analysis Lab
KNUST
woappaw.cos@knust.edu.gh
Presentation overview

1) Overview of the current state of the scientific evidence linking Aflatoxin to child growth

2) What are the criteria needed to decide that aflatoxin cause stunting

3) What are the possible solutions?

4) Conclusion
The problem-----Chronic Malnutrition

- 165 million <5 are stunted
- Growth retardation in young children associated with:
  - delays in cognitive development,
  - lower school achievement,
  - lower earnings and a higher probability of non-communicable chronic diseases at adulthood.

Current evidence on most effective way to reduce stunting:
- Scale-up interventions to prevent (rather than treat or reverse) stunting
- First 1,000 days (i.e. from conception to 24 months of age), “window of opportunity to prevent stunting”
- Scaling up of 10 proved nutrition-specific interventions to cover 90% of stunted will reduce stunting by 20% ONLY?? (Lancet 2013)

Several Research efforts are focusing on identifying presently unknown causes of growth retardation!!!!

Mycotoxins (e.g. Aflatoxin is one of those UNKs)
What are Aflatoxins

- Aflatoxins are toxins produced by *Aspergillus* fungi which infect maize, groundnuts, wheat, and many other staple foods.

- They are class 1 carcinogen (IARC)

- Drought stresses crops, Pest infestation also increase infection rates

- Control of toxin happen pre-harvest (e.g. Aflasafe) or post-harvest good agronomy practices (e.g. good drying practices and proper storage minimizing moisture.)
Table 1. Limits of aflatoxin growth and production by *A. flavus* and *A. parasiticus*

<table>
<thead>
<tr>
<th></th>
<th><em>A. flavus</em></th>
<th><em>A. parasiticus</em></th>
<th><em>A. flavus</em></th>
<th><em>A. parasiticus</em></th>
<th><em>A. flavus</em></th>
<th><em>A. parasiticus</em></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Minimum</td>
<td>Optimum</td>
<td>Maximum</td>
<td>Optimum</td>
<td>Maximum</td>
<td>Optimum</td>
</tr>
<tr>
<td>Temperature °C</td>
<td>10-12</td>
<td>12</td>
<td>33</td>
<td>32</td>
<td>43</td>
<td>42</td>
</tr>
<tr>
<td>Water activity</td>
<td>0.8</td>
<td>0.80-0.83</td>
<td>0.98</td>
<td>0.99</td>
<td>&gt;0.99</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>pH</td>
<td>2</td>
<td>2</td>
<td>5-8</td>
<td>5-8</td>
<td>&gt;11</td>
<td>&gt;11</td>
</tr>
<tr>
<td>Aflatoxin production</td>
<td>Minimum</td>
<td>Optimum</td>
<td>Maximum</td>
<td>Optimum</td>
<td>Maximum</td>
<td>Optimum</td>
</tr>
<tr>
<td>Temperature °C</td>
<td>13</td>
<td>12</td>
<td>16-31</td>
<td>25</td>
<td>31-37</td>
<td>40</td>
</tr>
<tr>
<td>Water activity</td>
<td>0.82</td>
<td>0.86-0.87</td>
<td>0.95-0.99</td>
<td>0.95</td>
<td>&gt;0.99</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>pH</td>
<td>--</td>
<td>2</td>
<td>--</td>
<td>6</td>
<td>--</td>
<td>&gt;8</td>
</tr>
</tbody>
</table>

**Source:** (ICMSF, 1996).
AFLATOXIN IS POISONOUS

Aflatoxin, a byproduct of naturally-occurring fungi that infect many crops, is a Class 1 Human Carcinogen and leads to:

- Liver Cancer
- Immunosuppression

10% of adult deaths in Southeast Asia and Sub-Saharan Africa are caused by liver cancer.

- Stunting
- Mental Impairment
- Acute Poisoning

Up to 35% of child stunting is associated with aflatoxin.

- Contaminated Meat & Milk
- Passed to Human Consumers

AFLATOXIN IS HARMFUL TO ECONOMIES

Higher medical costs, market losses and toxic effects in livestock can devastate economic systems and livelihoods.

In 2001, Africa lost over $600 million in trade with the E.U. due to aflatoxin contamination.

$1 billion USD per year estimated cost of aflatoxin management in the Philippines, Thailand and Indonesia.

25% of the world’s crops are susceptible to aflatoxin.

CAUSES

- Pre-harvest infection
- Insufficient grain drying
- Poor storage
- Contaminated meat/milk/eggs

PREVENTION

- "Aflasafe" is a harmless fungus that competes with and prevents the growth of the aflatoxin-producing fungus in the field.
- "Plant breeding" through traditional and biotech-driven methods can produce aflatoxin-resistant crops.
- "Stove and solar powered grain dryers" reduce moisture content before storage, which reduces the capacity for fungal growth.
- "Low-cost hermetic storage bags" last up to a full year and eliminate the need for pesticides, prevent infestation and stop mold growth.
- Adequate testing can ensure that animal feed is not contaminated at dangerous levels. Chemical binding agents and food processing techniques are currently being studied to establish efficacy.

HOW DO WE ENSURE SMALLHOLDER ACCESS TO PREVENTION TECHNOLOGIES?

Learn more at agrilinks.org/aflatoxin

*Aflatoxin interventions supported by the U.S. Agency for International Development through Feed the Future. Feed the Future is the U.S. Government’s cornerstone global hunger and food security initiative, and supports broad-based economic growth through agricultural development with a focus on enabling smallholder farmers to increase productivity of better, more nutritious foods. Learn more: www.feedthefuture.gov
What do we know about Aflatoxins toxicity?

- **Acute Exposure**
  
  If large doses are eaten, it will cause rapid death (e.g. Aflatoxicosis; Kenya 2004, 317 cases of reported death)

- **Chronic exposure**
  
  - Chronic exposure to low doses Cause of liver cancer
  
  - May Cause child stunting and low birth weights in animals and humans!!!!
How do we get exposed to Aflatoxins:

- Aflatoxin present in dried foods; human breast milk; cow milk, poultry, eggs, and meat if animals given feed with aflatoxins.

- Child exposure risk increases after weaning

- Dependence on single commodity with little diet diversity increase the risk of exposure significantly
**Studies linking aflatoxin to growth impairment in children—Just an example of the evidence!!**

<table>
<thead>
<tr>
<th>Type of study</th>
<th>Results</th>
<th>Nation &amp; study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aflatoxin measurements in stored flour, rural homes</td>
<td>Stunting, underweight, &amp; wasting associated with higher AF levels in flour</td>
<td><em>Kenya</em> (Okoth &amp; Ohingo 2004)</td>
</tr>
<tr>
<td>Cross-sectional: AF-alb levels in maternal, cord, child blood</td>
<td>Stunting &amp; underweight associated with higher AF-alb levels in these fluids</td>
<td><em>Togo, Benin, United Arab Emirates, The Gambia</em> (Gong et al. 2002*, Abdulrazzaq et al. 2004, Turner et al. 2007)</td>
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<tr>
<td>Longitudinal: AF-alb levels in children’s blood</td>
<td>Reduced height gain in 8 mos associated with AF-alb levels</td>
<td><em>Benin</em> (Gong et al. 2004)</td>
</tr>
<tr>
<td>AFM1 in mothers’ breastmilk</td>
<td>Lower length at birth &amp; in infancy associated with AFM1</td>
<td><em>Iran</em> (Sadeghi et al. 2009, Mahdavi &amp; Nikhniaz 2010)</td>
</tr>
</tbody>
</table>

*Dose-response relationship between AF-alb & HAZ, WAZ

• Gong et al (BMJ, 2002) showed that **stunting** and **weight for age** was inversely related to aflatoxin levels in Gambia. Jolly and colleagues (Peanut Innovation Lab) have shown the same in Ghana.
How does Aflatoxin cause stunting? **Exact Mechanism is still missing**; however several has been proposed:

1) **Immunomodulation associated with aflatoxin exposure** (Bondy and Pestka, 2000; Turner et al., 2003) ---cause recurrent infections in children, which can lead to growth impairment (Gong et al., 2008)

2) **Changes in intestinal integrity** (possibly in part resulting from immunomodulation) could make hosts more vulnerable to intestinal foreign microbes (Gong et al., 2008)

3) **Downregulation of genes associated with energy production and fatty acid metabolism** (Yarru et al., 2009)

4) **Impairment of protein synthesis and the inability to mobilize fat** (Kocabas et al., 2003)

5) **Changes in hepatic metabolism of vitamins and micronutrients** (Schaeffer and Hamilton, 1991).
Together with DON and fumonisin, might lead to environmental enteropathy
Interventions to reduce aflatoxin risk

- **Preharvest**
  - Good agricultural practices
  - Genetically enhancing plants’ resistance
  - Biocontrol
  - Biotechnology/breeding

- **Postharvest**
  - Improved sorting, drying, food storage
  - Crops not prone to aflatoxin (e.g. Soybean)

- **Dietary**
  - Improved dietary diversity
  - Dietary enterosorbents
  - Dietary chemoprevention
    - Curcumin
    - Compounds in cruciferous & Allium vegetables
    - Green tea polyphenols

Hepatitis B vaccine:
- Aflatoxin consumption in HBV+ patients increase risk of Liver cancer

Food additives:

- “Enterosorbents” trap aflatoxins in the gut
- E.g. Calcium montmorillonite clay (marketed as NovaSil)

Evidence on efficacy:
- Ghanaian adults given a placebo, either a 1.5- or 3-gram clay capsule; Daily for three months;
- Net reduction in serum aflatoxin levels of 21% and 24%.

Remaining questions and concerns:
- Effect large enough to reduce negative effects on linear growth?
- To what extent does clay also bind micronutrients and lead to micronutrient deficiencies?
Chemopreventive agents:

- Chlorophyllin (a derivate of chlorophyll) and oltipraz (an antischistosomal drug);
- Intervene in the biochemical pathway linking liver cancer to aflatoxin exposure;
- Whether effective in stunting pathway is unknown. Important concern for use of both enterosorbents and chemopreventive agents:

Important concern for use of both enterosorbents and chemopreventive agents:

- Should not be interpreted as a substitute for good crop agronomy
- Should not unintentionally encourage the use of foods not fit for human consumption.
What does this mean?

- Eliminating stunting & malnutrition will require provision of adequate and diverse diets; removing environmental contamination (e.g. Aflatoxin); preventing infectious diseases. Why these?

- Systematic review of nutrition programs: very best programs only deal with ~ 1/3rd of stunting at best

- Stunting is strongly related to foodborne toxins (such as Aflatoxin), etc.
Conclusions

- **Aflatoxin relation with Stunting?**
  - It is strongly associated with it and likely a cause

- **What is needed next?**
  - Controlled experimental studies urgently needed.

- **Is USAID doing anything to add to the evidence base?**
  - Yes; 1) The Nutrition Innovation lab studies in Nepal and Uganda 2) The SHINE trials in Zimbabwe

- **Are we doing enough?**
  - NO; This is a Global health and an Agriculture issue that is equally important to both sectors and GH community needs to engage actively to add to the evidence base and find solutions
- Will Aflatoxin reduction improve the health problems associated with stunting e.g. cognition problems?
  - We don’t know

- Should we wait to take an action for more evidence?
  - Absolutely not; we have enough evidence from animal and human studies and we need to take actions urgently.
Can one entity Do it all alone?

No

Implementing aflatoxin control interventions need extensive involvement from multiple stakeholders, from the levels of individuals to national and international institutions.

Leroy J. 2013
Thank you