Aflatoxin Impacts on Child Growth

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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
Lancet 2013

- 10 targeted interventions implemented at 90% coverage cuts stunting by 20%, mortality by 15%.

- But…“coverage rates for [many] interventions are either poor or non-existent.”

- Cost: US$9.6 billion per annum.

- Even at 90% coverage, 80% of stunting remains!!!
80% Nutrition Sensitive Interventions

20% Nutrition specific interventions
80% Nutrition Sensitive Interventions

- Agri. Technologies?
- Educations and BCC
- Up to 35% or more WASH
- Up to 35% Mycotoxins
- Conditional Cash Transfer Linked to Nutrition interventions?
- Social Safety nets/ transfer

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Climate change?

Educations and BCC

Agri. Technologies?

Up to 35% or more WASH

Up to 35% Mycotoxins

Conditional Cash Transfer Linked to Nutrition interventions?

Social Safety nets/ transfer

Up to 35% or more Mycotoxins

Policies?
Working together (i.e. Not one approach can do it all) ?

Could we achieve the 100%??
Do no harm (malaria, bird flu, pesticides)
Empowerment, income control (Women Emp.)

Tradeoffs; opportunity costs of time

Diet quality (animal source foods, whole diet diversity; anti-nutrients in meals)

Environmental enteropathy (gut microbiota; shared pathogens)

Caloric, protein and micronutrient intake
Nutritional status
Food safety (mycotoxins; cytokines)

Source: Masset et al. 2011
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)
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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.

- 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.)
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**!!!!
Suggested by:
- Evidence from human and animal studies
- Current knowledge of the biological mechanisms of action of aflatoxin

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>Kenya (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>Togo, Benin, United Arab Emirates, The Gambia (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>Benin (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>Iran (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).
Aflatoxin along with DON and fumonisins, might lead to environmental enteropathy.

Impaired Growth
Points of Control of Aflatoxin
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?
• 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 ~ $1/3$rd 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.

- 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
Is USAID doing anything to add to the evidence base?

Yes; The next couple of slides shows some examples from Feed the Future.
Examples of Feed the Future programs

Key Washington Research Projects

ARP:
• Peanut/Mycotoxin Innovation Lab
• Nutrition Innovation Lab
• NBCRI with USDA/ARS
• Venganza Research Grant
• KSU Post Harvest Innovation Lab
• Purdue Food Processing Innovation Lab

MPI:
• AflaSTOP Post Harvest Storage Structures
• AgResults Nigeria pilot project

Africa Bureau:
• Regional East Africa for Aflasafe
Key Field Mission Projects

- **EA Regional:**
  1. Aflatoxin Policy and Program for East African Region (APPEAR)
  2. Aflasafe Utilization in 11 countries (Kenya, Ghana, Nigeria 1st) with IITA and BMGF;
  3. Support for EAC Aflatoxin Policy and Action Plan

- **Kenya/Ghana/So. Africa (SPS Capacity Building)**
- **Zambia (Maize/Groundnuts: Biocontrol)**
- **Mozambique (Maize/Groundnuts: Biocontrol)**
- **Rwanda (Maize/Cassava: Biocontrol)**
- **Malawi (Maize/Groundnuts – Biocontrol)**
- **Tanzania (Maize – Prevalence/Markets)**
- **Afghanistan-Mycotoxin Assessment study**
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.
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
www.feedthefuture.gov

@feedthefuture

Thank you
Chemopreventive agents:

- Chlorophyllin (a derivate of chlorophyl) 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:

Wu F & Khlangwiset P (2010)