Toxins that harm children

• Dr. David Githanga
• KPA Annual Scientific Conference
• Pride Inn Paradise Mombasa
• 25th April 2018.

• “I Have nothing to declare”
Vulnerable Groups
Poverty!!!

• The most pressing moral/political/economic issues of our lifetime
• Makueni county has poverty level of 60.6% (National average 45.2%)
• Morally unconscionable

• Inequality is the gorilla in the room
• Inequity between and within countries requires urgent redressing: NOT Isolationism! Not even between counties
• Globalisation: ‘Every silver lining has a cloud’-
Your perspective determines your actions...

Population: Asset/Liability

Health Expenditure: Consumption/Investment

Health as Development: Essential Input/Outcome
Social Determinants of Health

• These are the circumstances in which people are born, grow up, live, work, and age, and the systems put in place to deal with illness (health).

• These circumstances are shaped by a wider set of forces:
  – economics, social policies, and politics
Source: Dahlgren and Whitehead (1991)
Natural Toxins in Foods

- **Endogenous toxins of plant origin**
  - Toxic phenolic substances: flavonoids, tannins, coumarin, safrole, and myristicin
  - Cyanogenic glycosides
  - Glucosinolates
  - Acetylcholinesterase inhibitors
  - Biogenic amines
  - Central stimulants

- **Natural contaminants**
  - Mixing of edible plants with toxic plants
  - Contamination resulting from intake of toxic substances by animals
  - Microbial toxins
Mycotoxin

• Common ones: aflatoxin, ochratoxin, deoxynivalenol/vomitoxin, zearalenone, fumonisins, T-2 toxin, trichothecenes, citrinin

• Aflatoxins and fumonisins - widespread exposure in humans (Williams 2004)
What are Aflatoxins?-’mbuuka’

- Toxins produced by the fungi *Aspergillus flavus* and *Aspergillus parasiticus*
  - Aflatoxins are secondary fungal metabolites.
  - Aflatoxin types include B1, B2, G1, G2.
  - B1 is most prevalent and toxic aflatoxin-hepatoma, cirrhosis.

Detection:
- Fluorescence can be used to detect presence of *Aspergillus* on crops
- Biomarkers are used to detect aflatoxin exposures in humans
Aflatoxins and Environmental Conditions

• Conditions favour aflatoxin formation by promoting aspergillus growth:
  • High temperature/humidity/organic content/moisture
  • Presence of external plant stressors:
    • drought-weaken seed kernels of plants; fungal contamination
    • Insect infestation
Chronic Aflatoxin Exposure and Human Health

• Carcinogenicity
  • Liver cancer long-term exposure to aflatoxins.
  • Hepatitis B infection exacerbates the effects of aflatoxin exposure. Hepatitis B vaccine mitigates carcinogenicity of the toxin.
• decreased immune and reproductive function.
• chronic exposure may experience growth failure.
  • Infants may be exposed through breast milk.
  • The fetus may be exposed during pregnancy if the mother consumes aflatoxins.

No level of aflatoxin exposure is considered safe for humans.
The drama with Aflatoxin

Acute aflatoxicosis that is **fatal**. Dependent on consumed quantity. Clinical symptoms in humans include:

- Abdominal pain
- Vomiting
- Pulmonary edema
- Liver necrosis
Aflatoxicosis in Kenya

- First documented - 1981
- Recent severe outbreaks
  - 2004-2006
  - Makueni and Kitui
  - 447 cases
  - 181 deaths
  - Case Fatality: 40%
- 2014 Oloitoktok
  - 27 suspected cases with
    - 10 deaths = CFR of 40%
- All outbreaks with consumption of homegrown maize
‘The iceberg below the tip’...

Chronic low dose exposure..

- decreased immune and reproductive function.
- Liver cancer.
- Hepatitis B infection worsens the effects of aflatoxin exposure.
- chronic exposure & growth failure.
- Infants exposed through breast milk.
- The fetus suffers transplacental spread
Aflatoxins and Food Production

Major crops affected by aflatoxins include maize (corn) and groundnuts (peanuts). Agricultural practices can be modified to reduce aflatoxin production / contamination.

Farming practices
- irrigation
- pesticide use
- time of harvest

Storage practices
- drying techniques
- processing, such as shelling peanuts
- exposure to pests

Aspergillus on maize

Drying maize
Aflatoxins in Farmed Animals

• Poultry
  – Highly sensitive
  – Aflatoxin toxicity impairs uptake of essential nutrients as well as causing tissue damage

• Ruminants
  – Ruminants are relatively insensitive; however, aflatoxin exposure can cause growth impairment in young or lactating animals.
  – Metabolites in milk and related dairy products
    • Aflatoxin consumed by cows is excreted in milk as the M1 metabolite.
    • The M1 metabolite can be absorbed by calves or humans causing growth failure.
    • The M1 metabolite also remains present in milk-based products such as cheese and yogurt.

• Fish
  – When farmed fish are accidentally fed contaminated grains, large die-offs may occur.
    • Rainbow trout are highly sensitive

Animal deaths and reduced productivity from aflatoxin exposure can have significant negative ‘economic’ impact in addition to the negative health outcomes for those who consume contaminated animal products.
I get by with a little help....asante!
Allowable Aflatoxin Levels in Human Foods

<table>
<thead>
<tr>
<th>Amount</th>
<th>Food type</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 ppb</td>
<td>Foods in general</td>
</tr>
<tr>
<td>0.5 ppb (aflatoxin M1)</td>
<td>Milk</td>
</tr>
<tr>
<td>20 ppb</td>
<td>Peanuts and peanut products</td>
</tr>
<tr>
<td>20 ppb</td>
<td>Pistachio nuts</td>
</tr>
<tr>
<td>20 ppb</td>
<td>Brazil nuts</td>
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Kenya’s mortality pattern

- High morbidity and mortality in the paediatric population due to vaccine-preventable illnesses continues despite varied and exerted efforts.

Figure 3: Distribution of Causes of Death among Under Fives in Kenya

Distribution of causes of deaths among under fives in Kenya, 2000-2003

- Neuronal causes: 24%
- HIV/AIDS: 15%
- Diarrhoeal diseases: 14%
- Measles: 16%
- Malaria: 14%
- Pneumonia: 3%
- Injuries: 5%
- Others: 3%
- Unknown: 20%

Source: WHO, Kenya Mortality Country Fact Sheet 2006
Aflatoxin & immunomodulation

• In vivo & in vitro studies of animals & human cells (Gallikeev 1968, Pier, 1970)
• Modulate cytokine production (Oswald 2005, Bondy 2000)
• Decrease T or B lymphocyte activity
• Impair macrophage/neutrophil functions,
• Suppress NK cells-mediated cytolysis
• Depress immunity to vaccinations (Yi Jiang 2008)
Immunity...

• Most antigens and vaccines trigger both B and T cell responses.
• CD4$^+$ T cells are required for most antibody responses
• antibodies exert significant influences on T cell responses to intracellular pathogens. (Igietseme JU, et al 2004).
Immunotoxicity in humans

• Threshold dose unknown

• 2 main studies in West Africa (Turner PC 2003; Jiang 2005)

• “limited, inconsistent and uncertain”
Random selection of 410 subjects 1-14 years

- Not vaccinated
- Vaccinated

Consenting subjects

Excluded

Excluded

Questionnaire

Blood counts
Antibody levels
Cytokine levels
Liver function tests
Aflatoxin in blood/grain
Urine fumonisin
Stool helminths

Analysis of data

Schema of data collection by Dr. David Githanga
Serum aflatoxin levels

Frequency Distribution of AFB$_1$-Lysine

<table>
<thead>
<tr>
<th>AFB$_1$-Lysine (pg/mg albumin)</th>
<th>Count</th>
</tr>
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<tbody>
<tr>
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</tr>
<tr>
<td>5.0-9.9</td>
<td>83</td>
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<tr>
<td>10.0-19.9</td>
<td>85</td>
</tr>
<tr>
<td>20.0-49.9</td>
<td>123</td>
</tr>
<tr>
<td>50.0+</td>
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community buy-in...

Figure 14.1: Community attitudes to health
Doing nothing is a choice too..
Strategies for Reducing Aflatoxin Exposure

- Regulations
- Agricultural production quality control
- Food processing and crop storage safety
- Early recognition and medical management of health effects
- Educational outreach
  - Community
  - Individual
The Benefits of an Interdisciplinary One Health Approach

- Educating stakeholders on the interconnectedness of humans, animals and the environment is the first step in preventing aflatoxin-related health issues
Challenges to aflatoxin issues

- No local lab capacity to test for aflatoxin in serum

- We do not know the threshold of aflatoxin levels where you would start to see health effects

- Coordination - cross-cutting/ Multi-sectoral

- Replacement - withdrawal of contaminated food

- Rapid diagnostic kits at the sub-county level for early detection of aflatoxin contamination and for surveillance.
Human Consumption Recommendations

• Exposure reduction
  – Dietary modification
    • Diet diversity reduces aflatoxin exposure and improves overall human nutrition
    • Dramatic dietary alterations may not be affordable or culturally acceptable in many areas

• Education on sources of aflatoxin can alert consumers to risks
Recommendations continued..

• Post-exposure management
  – Hepatitis B vaccination
    • This intervention can be funded and implemented by governments without burdening growers; ensure coverage
  – NovaSil™ clay
    • Prevents intestinal uptake through adsorption of aflatoxins

• Prevention is the primary long-term goal
Outbreak response-recommendations

- Enhance multi-sectoral collaboration - through the Outbreak Control Team / Emergency Operating Center
- Regional reference lab should be established

- Public Private Partnerships

- Resources are needed to quantify the burden of disease and associated health effects
- Develop a food monitoring system (in foods and of jaundice (ongoing) - Early Warning System)
Human Health Recommendations

- Post-exposure management
  - Hepatitis B vaccination
    - Decreases rates of liver cancer
    - Complementary to decreasing aflatoxin exposure
    - This intervention can be funded and implemented by governments without burdening growers
  - NovaSil™ clay
    - Prevents intestinal uptake through adsorption of aflatoxins
- Prevention is the primary long-term goal
Challenges

- No local lab capacity to test for aflatoxin in serum
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- Coordination - cross-cutting/ Multi-sectoral
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Recommendation – Outbreak response

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Summary....

Aflatoxin

4 main aflatoxins- B_1, B_2, G_1, G_2, M_1
B_1, most toxic, abundant and potent carcinogen
Lipophillic crosses placental barrier
Maize: widely grown and consumed
Temps of 24-35 Celsius, moisture >7% favour aflatoxin production
Allowable levels for human food 4-30ppb, animals 300ppb
Expected worsening with the global warming
Primordial prevention is key
It perhaps contributes to LIC morbidity/mortality
Concerted multisectoral approach for mitigation

David Githanga (IITA Conference Mombasa April 2018)
I cannot believe that the purpose of life is to be “happy.” I think the purpose of life is to be useful, to be responsible, to be compassionate. It is, above all, to matter: to count, to stand for something, to have made some difference that you have lived at all.’

(Leo C. Rosten)
acknowledgement

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