

#### Biological mechanisms linking agriculture to nutrition: Role of food safety in achieving optimal health and well being in developing countries

**Date/Title/Additional Information** 

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## INTRODUCTION

- Within the context of the SDGs, food based approaches are an important programmatic strategy in improving nutrition and reducing mortality.
- Conversely, food-borne diseases account for 33 million DALYs and 420,000 deaths.
- Poor food safety reduces agricultural output, affects prices and trade in a global market.
- Emerging evidence on mycotoxins and environmental contamination and their relationship with nutritional status- stunting





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- Poor food safety: Implications for nutrition, food security, food policy and trade- Patrick Webb
- Food safety along the value chain: potential intervention strategies- Ahmed Kablan
- Environmental Enteropathy, Microbiome, Mycotoxins and Stunting- Shibani Ghosh
- Biological Markers for Mycotoxins and Selecting an Appropriate Study Design- Johanna Andrews-Trevino
- Group Discussion
- Assignment of Case study (Lunch)
- Post lunch discussion







## **ASSIGNMENT QUESTIONS**

- Select your own group, select a rapporteur
- Review the methodology paper any key issues or disagreements?
- In-group discussion to determine 1 top food safety priority needing research
- What research appropriate/method would you use?
- If planning an intervention study, how would you plan it to study efficacy/ impact
- Based on your discussion, present what you'd research, why, and how.







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# Poor food safety: Implications for nutrition, food security, food policy and trade

Patrick Webb

Nutrition Innovation Lab July 2017







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- 1. *Opportunity*: Food safety **new focus** of food/nutrition security.
- 2. *Challenge*: Nutrient-rich foods most valuable (for nutrition, as well as for nutrition), but **most perishable**!
- 3. *Policy implications*: **Actions needed across sectors**, with large private sector responsibility.
- 4. *Research needs*: Scale, nature, mechanisms, solutions.







"Food safety is a hidden, and often overlooked, problem. The pool of those people at greatest risk of disease is expanding."

We must align "policies in agriculture, trade, health, education, and social protection to provide a safe and healthy diet for all."

Margaret Chan, former DG of WHO – Lancet 2014 (Nov 29 issue)







#### Figure 1: Global Burden of Foodborne Disease (DALYs)





Source: Global Panel 2016







Source: Global Panel 2016





#### Documented food-based hazards

- Milk, kale East Africa (bacterial contamination)
- Fish products Bangladesh (formaldahide)
- Peppers, maize Nepal (aflatoxins)
- Groundnuts Uganda (mycotoxins)
- Green leafy veg India (toxic herbicides)
- Street foods SE Asia (e-coli)







#### Global food trade: access to nutrient-rich foods



United States International Trade Commission

Trans-Pacific Partnership Agreement: Likely Impact

TPP would benefit trade in fresh fruits, vegetables and nuts, currently hampered by sanitary and phytosanitary restrictions.

> May 2016 Publication Number: 4607 Investigation Number: TPA-105-001







#### Recommendations

- Strengthen evidence-base on hazard risk to vulnerable consumers to define appropriate economic actions.
- Food trade regulations focus on nutrition, not only income.
- Establish context-appropriate regulations (not blanket prescriptions than may hurt nutrition)
- Much to be gained via new technologies to reduce perishability in storage, marketing, retail.
- > Promote 'safe' **diet diversification** (via consumer knowledge).







Food systems are evolving, giving rise to new food safety challenges. Assuring a safe food supply requires the highest level of political commitment to strengthen national systems. This is especially important for Africa and other developing countries.

Akinwumi Adesina, President, African Development Bank







# Food safety along the value chain: potential intervention strategies

#### Ahmed Kablan, PharmD, PhD.

Senior Nutrition and Public Health Research Adviser

Bureau for Food Security/ Office of Agriculture Research and Policy USAID



#### **Agriculture Influenced**











#### **Food Safety System Across the Value Chain**





• System biology:

Identify /know the risk (e.g. toxigenic Asp. Spp in soil; type of microbes of potential risk to meat/diary products..etc)

- Understand the basic genetic component of pathogens
- Expression



- Detection & Dx. of contaminants (DX)
  - In soil
  - In raw materials
  - During processing
  - Should be sensitive & Specific
  - Can detect as early as possible (avoid future recalls, passing of harmful food to consumer...etc)



- Intervention & Control methods and strategies
  - Biocontrol /Afalasafe
  - GAP (irrigation, mulching, fertilizers..etc)
  - Clean slaughter houses
  - Methods to dispose of by products after harvest (blood, hair..etc)
  - Clean/appropriate collection containers



- Population Systems
  - Movement, dynamics, structure & characteristics of the population throughout the food production system
  - Food processing and storage
  - Interaction with food including epidemiology, ecology, host-pathogens relationships



#### **Post-Harvest**

- Drying /moisture: grains mainly
  - Relative humidity (RH) <65% no mold./fungal growth , <35% no pest growth</li>
  - Speed & rate of drying is important to stop potential mold growth and production of toxins



#### **Post-Harvest**

- Storage
  - Cold storage
    - F&V, Meat, Poultry , fish
    - Timing and speed and temp is critical
    - Food spoilage could happen at 1-2 degrees above recommended temp
    - Long term should be frozen
- Ambient Temp storage
  - Hermitic storage , avoid increase in RH, protect from pest infestation , prevent the diffusion in humidity



#### **Post-Harvest**

• **Sorting** : to remove any contaminated /infected crops

• E.g. hand sorting of moldy peanuts is highly effective at reducing aflatoxin exposure





#### Shipping/transport

- Appropriate temperature control during transport
- Sanitation & hygeine (Pest, Personal,
- Appropriate packaging/packing of food products
- Good communications between shipper, transporter and receiver
- Employee awareness and training.







The time course of aflatoxin formation and reduction in peanuts, with reference to the Food Safety Objective.

J.I. Pitt et al. / Food Control 32 (2013) 205e215



#### Processing/Preparation (HH, Commercial)

- Final & important step esp. in LMIC
- Proper hygiene during food preparation & Serving is critical to prevent cross contamination
- Proper preparation and cooking temp





# Thank you



#### Environmental Enteropathy, Microbiome, Mycotoxins and Stunting

#### Shibani Ghosh

July 9, 2017







#### **GLOBAL NUTRITION TARGETS FOR 2025**



**ADULT DIABETES** 

(high blood sugar)

World Health Assembly Global Nutrition Targets- 2025 and Global Monitoring Framework for Prevention and Control of NCDs

http://ebrary.ifpri.org/utils/getfile/collection/p15738coll2/id/130354/filename/130565.pdf

**ADULT OVERWEIGHT** 





ADULT OBESITY



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#### Prendregast and Humphrey, 2014



Figure 1 The stunting syndrome. The green pathway denotes the period between conception and 2 years ('the first 1000 days')



#### ENVIRONMENTAL ENTEROPATHY

- Sub-clinical disorder of the small intestine
- Phenomenon of impaired intestinal function rather than a clinical condition
- Environmental exposure to infections and enteric pathogens- early in life- gut in perpetual state of low level inflammatory immune stimulation
- Over time- disruption of normal intestinal function, alterations in mucosal lumen surface structure, compromise in gut capacity to absorb nutrients





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## MICROBIOME

- The intestinal microbiota is an ecosystem of gut microbes
- helps to modulate nutrient harvesting from the diet, mucosal inflammation, and the immune response in the gut







Fig. 1. The intestinal epithelium in health (a) and with environmental enteric dysfunction (b). Adapted and reprinted with permission from Macmillan Publishers Ltd. Nature Reviews Microbiology: Sandler and Douek (2012).

#### **Review Article**

Preventing environmental enteric dysfunction through improved water, sanitation and hygiene: an opportunity for stunting reduction in developing countries

#### Mduduzi N. N. Mbuya<sup>\*,†</sup> and Jean H. Humphrey<sup>\*,†</sup>

\* Zvitambo Institute for Maternal and Child Health Research, Harare, Zimbabwe, and <sup>†</sup>Johns Hopkins Bloomberg School of Public Health, Baltimore, Mayland 21 205, USA



# ENVIRONMENTAL ENTEROPATHY (EED)

- LM Test (Lactulose mannitol dose and excretion in urine)
- EED testing in Uganda (lactulose:mannitol): **385 children 12-16 m**.
  - Median L:M score 0.27: 21% no EED, 58% moderate, 22% severe.
  - Infants with clean water better L:M scores (P<0.050).</p>
  - ➢ If goats/sheep inside home, significantly worse L:M (P<0.050).</p>
  - L:M significantly higher if infants stunted or wasted at 6-9m (i.e. prior to L:M test).
- Fecal markers- myeloperoxidase, npeoterin, AAT (alpha 1- antitrypsin), inflammatory markers- cytokines, interleukins, immunoglobulins, calprotectin, zonulin
- Blood markers- serum flagellin, serum citrulline, serum lipopolysaccharide
- Fecal MRNA







# Malnourished Children have less diverse, different gut microbiomes



Gupta et al. Gut Pathogens 2011, 3:7 http://www.gutpathogens.com/content/3/1/7

#### Gut Microbiomes of Malawian Twin Pairs Discordant for Kwashiorkor

Michelle I. Smith,<sup>1</sup>\* Tanya Yatsunenko,<sup>1</sup>\* Mark J. Manary,<sup>2,3,4</sup> Indi Trehan,<sup>2,3</sup> Rajhab Mkakosya,<sup>5</sup> Jiye Cheng,<sup>1</sup> Andrew L. Kau,<sup>1</sup> Stephen S. Rich,<sup>6</sup> Patrick Concannon,<sup>6</sup> Josyf C. Mychaleckyj,<sup>6</sup> Jie Liu,<sup>7</sup> Eric Houpt,<sup>7</sup> Jia V. Li,<sup>8</sup> Elaine Holmes,<sup>8</sup> Jeremy Nicholson,<sup>8</sup> Dan Knights,<sup>9,10</sup>† Luke K. Ursell,<sup>11</sup> Rob Knight,<sup>9,10,11,12</sup> Jeffrey I. Gordon<sup>1</sup>‡

#### Science 339:548-554. 1 February 2013

- 317 Malawian twins studied first 3 years of life
- 50% both well nourished; 43% <u>discordant</u> (one well, one malnourished); 7% both were malnourished.
- Both twins in discordant pairs received RUTF, a therapeutic food. Gut microbiomes (MB) studied: RUTF → transient MB improvement.





## MICROBIOME AND STUNTING

- Less diverse gut microbiota are associated with stunting severity
- Increase in the relative abundance of Acidaminococcus sp. associated with lower future linear growth in Malawi and Bangladesh



Gough et al. Microbiome (2015) 3:24 DOI 10.1186/540168-015-0089-2



RCH

Linear growth faltering in infants is associated with *Acidaminococcus* sp. and community-level changes in the gut microbiota

Ethan K. Gough<sup>1</sup>, David A. Stephens<sup>2</sup>, Erica E.M. Moodie<sup>1</sup>, Andrew J. Prendergast<sup>34</sup>, Rebecca J. Stoltzfus<sup>5</sup>, Jean H. Humphrey<sup>46</sup> and Amee R. Manges<sup>27</sup>





Review Article

Preventing environmental enteric dysfunction through improved water, sanitation and hygiene: an opportunity for stunting reduction in developing countries

Mduduzi N. N. Mbuya\*,† and Jean H. Humphrey\*,†

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Fig. 2. Biological mechanisms linking environmental contamination, environmental enteric dysfunction and linear growth impairment.



- In EED, reduced intestinal barrier function enables bacterial translocation to occur, leading to chronic systemic inflammation, which is associated with malnutrition (acute and chronic)
- Increase in glutamate fermentation
- Glutamate important precursor for synthesis and metabolic recycling of other amino acids (e.g. arginine)
- Contributes to epithelium restitution, preserves barrier function, attentuates intestinal tissue damage





Ethan K. Gough<sup>1</sup>, David A. Stephene<sup>2</sup>, Erica E.M. Moodie<sup>1</sup>, Andrew J. Prendergast<sup>14</sup>, Rebecca J. Stoltzfus<sup>6</sup>, Jean H. Humphrey<sup>46</sup> and Amee R. Manges<sup>77</sup>







## CONCLUSION

- Mechanistic pathways from contamination/ingestion of contaminants such as aflatoxins, alterations in microbiome and recurrent infections leading to inflammation seem to be similar
- Implementing the 10 Lancet interventions at 90% coverage reduces stunting by only 20%
- Impacts of EED and poor microbiome could negate any gains made in program implementation







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# Biological Markers for Mycotoxins and Selecting an Appropriate Study Design

#### Johanna Y. Andrews-Trevino

July 9, 2017







## **MYCOTOXINS**

- Metabolites of fungi, cancer, growth faltering, neural tube defects, renal diseases and immune modulation/suppression
- Aflatoxin B1 (AFB1), fumonisin (FUM), deoxynivalenol (DON) and ochratoxin (OTA).
- Maize, (AFB1, FUM), groundnuts, wheat, oats, rice, barley, milk, chilies and spices, OTA has also been isolated in infant formula and baby foods
- Contamination pre-harvest due to poor agricultural practices (soil contamination) or post-harvest at different points in the value chain due to poor storage and processing practices.















#### AFLATOXIN LEVELS HIGHER IN HIV (+) WOMEN AND THEIR INFANTS









## MYCOTOXINS – AGRICULTURAL OR PUBLIC HEALTH ISSUE?

- Mycotoxins toxic secondary metabolites produced by species of fungi growing on grains before harvest and in storage.
- Contaminate staple foods consumed by many of the poorest and most vulnerable populations in the world.
- Aflatoxin is a type of mycotoxin, Class I human carcinogen, most frequently studied.
- Although animal studies over the past decades have repeatedly shown an association between aflatoxin exposure and growth impairment in many animals, the evidence is lacking in humans.



#### POTENTIAL SOURCES OF MYCOTOXINS

Fig. 1.10. Decision tree for directing risk management decisions or actions based on environmental considerations and probability of fungal contamination in warm climates. Expected toxic effects in susceptible animals are given for each group of mycotoxins.



Source: Pitt et al. 2012



# CHALLENGES TO MYCOTOXIN RESEARCH

- Multiple strains and different food items (maize, groundnuts, wheat, rice, chilies) contaminated
- Food items are usually not contaminated with a single toxin
  - Bulk of the literature relating growth impairment to mycotoxin exposure focuses on aflatoxin-related stunting.
    - What about the co-occurrence with fumonisins? DON? OTA?
- No established bio threshold
- Biological pathways (e.g. compromised gut health, liver dysfunction, immunity)



# CHALLENGES TO MYCOTOXIN RESEARCH

- Difficulty separating the effects of mycotoxins from poor diet quality
- Ethical considerations
  - Aflatoxins are carcinogens that have the potential to contribute to a diversity of adverse health effects in humans, even at low concentrations
  - No established threshold
  - Fear
- Difficulty measuring levels in food



#### **BIOMARKERS**

Table 2. Summary of the most prevalent mycotoxins in Africa

	Mycotoxins			
	AF	FB	DON	ZEA
Origin	Aspergillus flavus and Aspergillus parasiticus [9]	Fusarium verticillioides [31]	Fusarium culmorum and Fusarium graminearum [31]	Fusarium graminearum and Fusarium crookwellence [30]
Types	$B_1, B_2, G_1, G_2, M_1, M_2$	FB1, FB2, FB3		
Accumulation	accumulate after harvest	location, climate, susceptibility of the plant to fungal invasion, insect damage, crop stress		
Primary food sources	nuts, spices, maize (corn), cacao, coffee, rice, milk	maize (corn)	wheat, barley, maize (corn)	maize (corn), wheat, barley, sorghum
Solubility	fat soluble	water soluble [16]	partially water soluble	
TDI, μg/kg bw/day	none	2 [32]	100 [33]	
PMTDI, µg/kg bw/day		2	1	0.5
Urine biomarker	AF-guanine adduct, AFM <sub>1</sub> , AFP <sub>1</sub> , AFQ <sub>1</sub> and AFB <sub>1</sub> -mercapturic acid [34]	FB1	DON glucuronide, DON + de-epoxydeoxynivalenol (DON-1)	$\begin{array}{l} ZEA + \alpha \text{-}zearalenol \\ (\alpha \text{-}ZOL) + \\ \beta \text{-}zearalenol (\beta \text{-}ZOL) \end{array}$
Blood biomarker	Serum/plasma AF-alb adduct [34]			
Breast milk biomarker	AFM <sub>1</sub> [5]			

Source: Lombard 2014



# STUDY DESIGN

**Descriptive:** tries to give a picture of what is happening, rather than trying to quantify a relationship.

- Qualitative
- Cross-sectional survey (incidence, prevalence, experience of a group)

Analytical: Try to quantify the relationship between two factors

- Experimental
  - Randomized (parallel or crossover)
- Observational analytical
  - Cohort, case control



#### **STUDY DESIGN**

Meet certain criteria for rigor

- Sample size
- Outcome measures
- Exposure or dose assessments time dependent
- Appropriate analyses (controlling for confounders)



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