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Photo: J K Griffiths 2012

Water, Sanitation, and the Prevention of Stunting: An Holistic View of Why Food Isn't Enough

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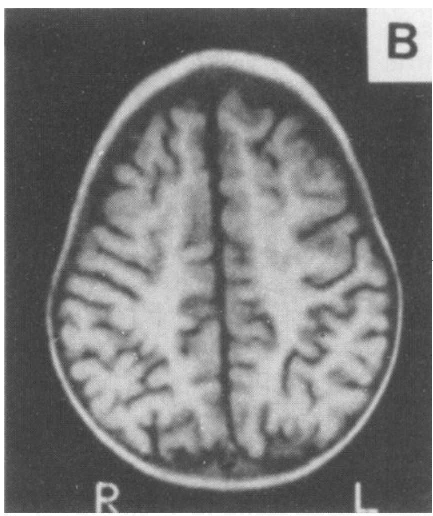
February 15, 2014

What is stunting, and why focus it?

- A stunted child is short for age (low "height for age"). A child that is $\leq$ 2 SD below his/her mean height for age ("HAZ $\leq$ -2") is stunted.
- Stunting is linked to: diminished scholastic achievement and intellectual function, reduced lifetime earnings, short adult stature, (and in women) adverse pregnancy outcomes.
- UNICEF 2013: 165 million children stunted… India: 48% of children. Yemen: almost 60%

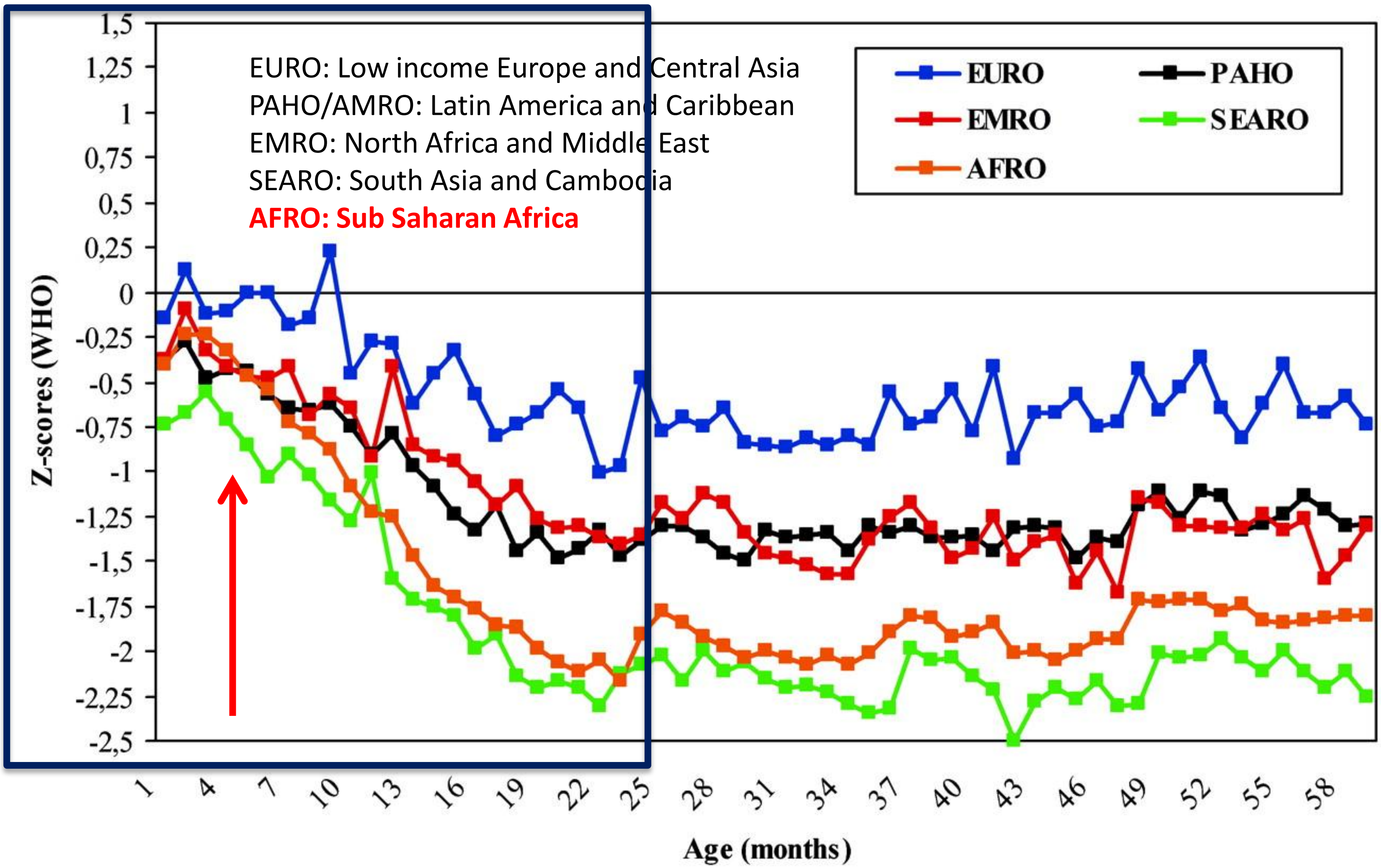
- Stunting reflects under-nutrition *in utero* and during infancy / early childhood - critical periods of physical and cognitive growth.



-Small Brain Volume (atrophy)
-Lower IQ when stunted children compared to non-stunted children

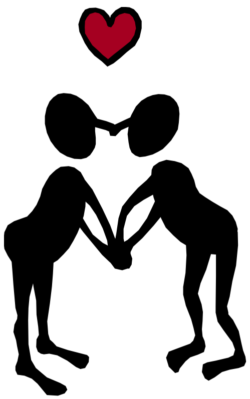
Same age girls in Bangladesh (UNICEF)

Window of Opportunity to end stunting: Pregnancy, and first 24 months of age



Mean height for age z scores by age, relative to the WHO standard, according to region (1–59 months). Victora C G et al. Pediatrics 2010;125:e473-e480

Nutrition Interventions (listed below) only address a minor portion of stunting



PREGNANCY

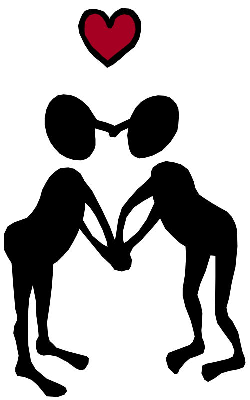
EARLY CHILDHOOD

ADOLESCENT, PRECONCEPTION, GESTATIONAL, AND MATERNAL NUTRITION
ADEQUATE CALORIES (PROTEINS, FATS, CARBOS) IN ALL LIFE STAGES
DIVERSITY OF MICRONUTRIENTS, VITAMINS, HIGH QUALITY PROTEINS
OPTIMAL BREASTFEEDING, RESPONSIVE FEEDING PRACTICES, STIMULATION
GOOD COMPLEMENTARY FEEDING 6-23 MONTHS, DIETARY DIVERSITY
WEALTH, EDUCATION – [BE SURE TO CHOOSE YOUR PARENTS WELL]
Others…..

FIX THESE: 20-33% STUNTING AVOIDED

Lancet 2013

Adequate and nutritious foods are *necessary but not sufficient.*



PREGNANCY

EARLY CHILDHOOD

MYCOTOXINS: FUNGAL FOOD TOXINS WHICH IMPAIR GROWTH AND IMMUNITY

ENVIRONMENTAL ENTEROPATHY:

INFLAMED, LEAKY, DYSFUNCTIONAL INTESTINES

THE GUT *MICROBIOME* - *GUT BACTERIA GONE BAD*

First, a focus on diarrheal disease

CONTAMINATED WATER AND FOOD; UNSANITARY ENVIRONMENT

As an infant is weaned, s/he is exposed to food and water which is contaminated. Children who crawl around on the floor eat and sample dirt, chicken poop, whatever. **Diarrhea**, other illnesses → **malnutrition**

Interventions for the control of diarrhoeal diseases among young children: improving water supplies and excreta disposal facilities*

S. A. Esrey,[1] R. G. Feachem,[2] & J. M. Hughes[3]

A theoretical model is proposed that relates the level of ingestion of diarrhoea-causing pathogens to the frequency of diarrhoea in the community. The implications of this model are that, in poor communities with inadequate water supply and excreta disposal, reducing the level of enteric pathogen ingestion by a given amount will have a greater impact on diarrhoea mortality rates than on morbidity rates, a greater impact on the incidence rate of severe diarrhoea than on that of mild diarrhoea, and a greater impact on diarrhoea caused by pathogens having high infectious doses than on diarrhoea caused by pathogens of a low infectious dose. The impact of water supply and sanitation on diarrhoea, related infections, nutritional status, and mortality is analysed by reviewing 67 studies from 28 countries. The median reductions in diarrhoea morbidity rates are 22% from all studies and 27% from a few better-designed studies. All studies of the impact on total mortality rates show a median reduction of 21%, while the few better-designed studies give a median reduction of 30%. Improvements in water quality have less of an impact than improvements in water availability or excreta disposal.

Bull WHO 1985

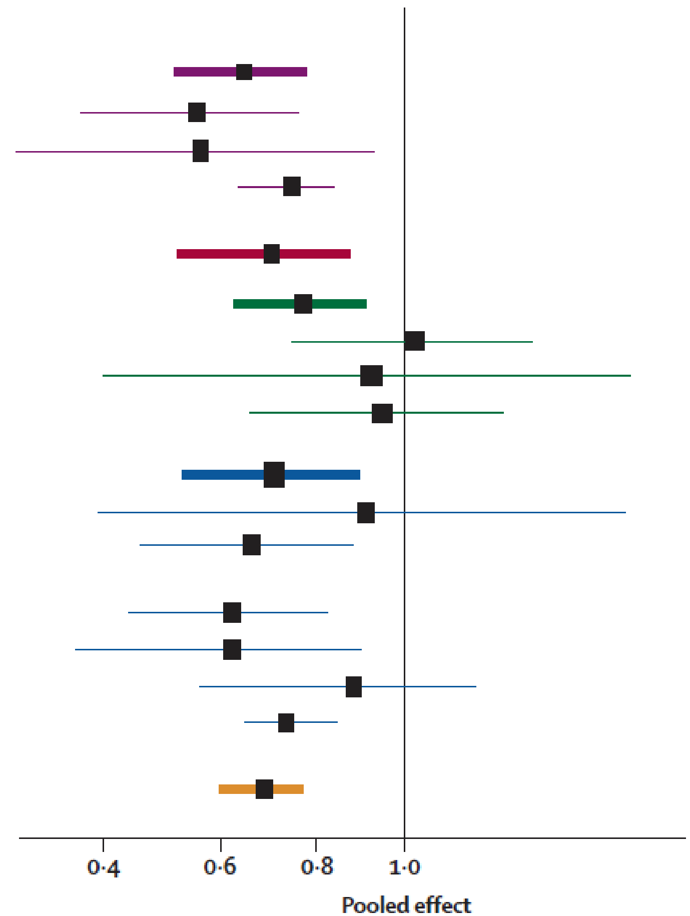
Impact on nutritional anthropometry. If water supply and excreta disposal improvements reduce diarrhoea incidence rates or duration among young children, then nutritional anthropometric indicators should also improve because of the inverse relationship between time spent with diarrhoea and child growth (*58, 68*). Six studies that investigated the relationship between water supply or excreta disposal improvements and nutritional status are summarized in Table 5. All six studies reported an association between improved water supply or excreta disposal and improved nutritional status. In two studies, in Fiji and the Philippines, attempts to control for extraneous risk factors reduced the differences between the control and intervention groups, but some of these differences were nonetheless found to be statistically significant.

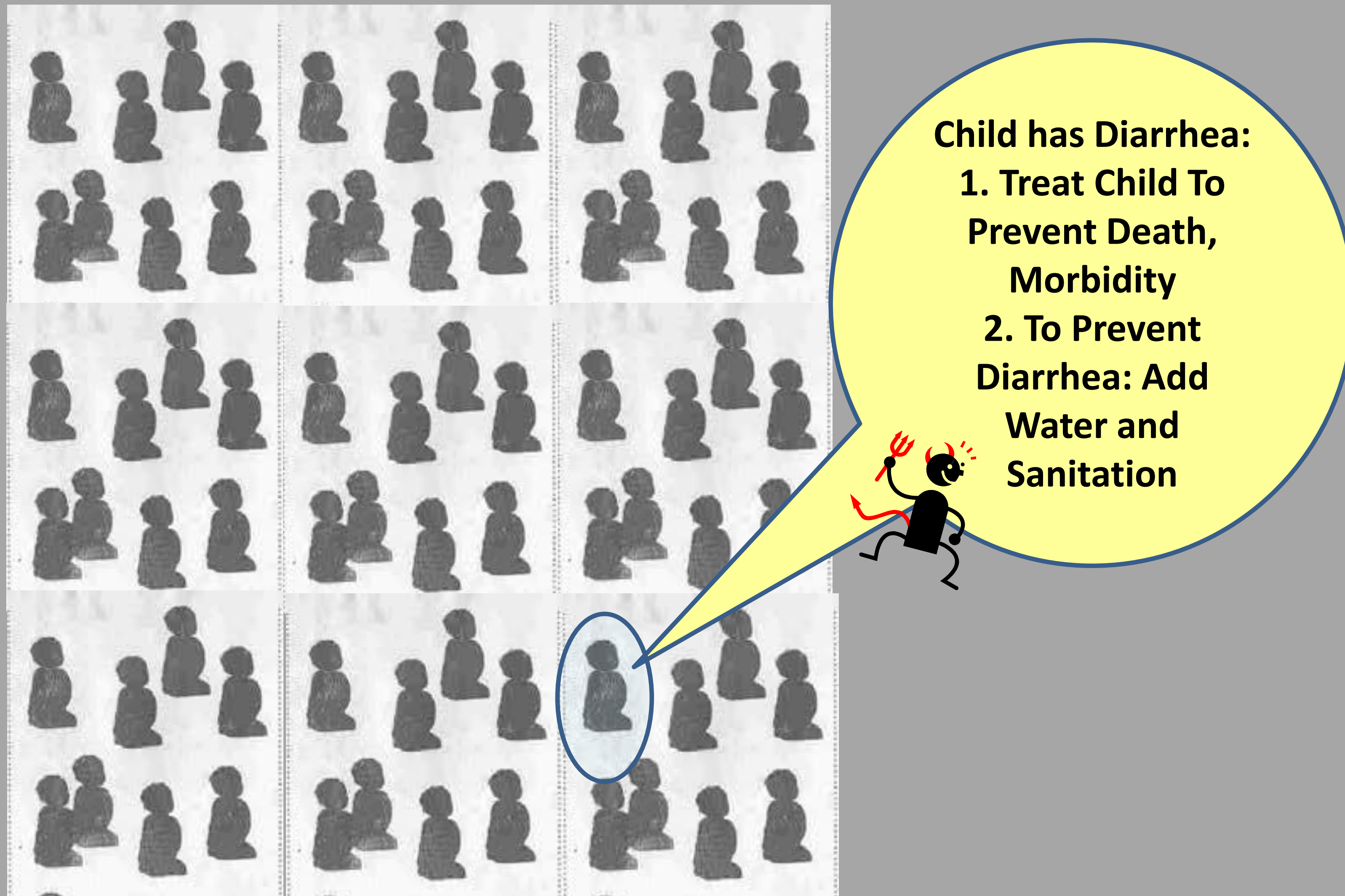
2005 Update: Water, sanitation, and hygiene interventions to reduce diarrhoea in less developed countries: a systematic review and meta-analysis

Lancet Infect Dis 2005; 5: 42–52

Lorna Fewtrell, Rachel B Kaufmann, David Kay, Wayne Enanoria, Laurence Haller, and John M Colford Jr

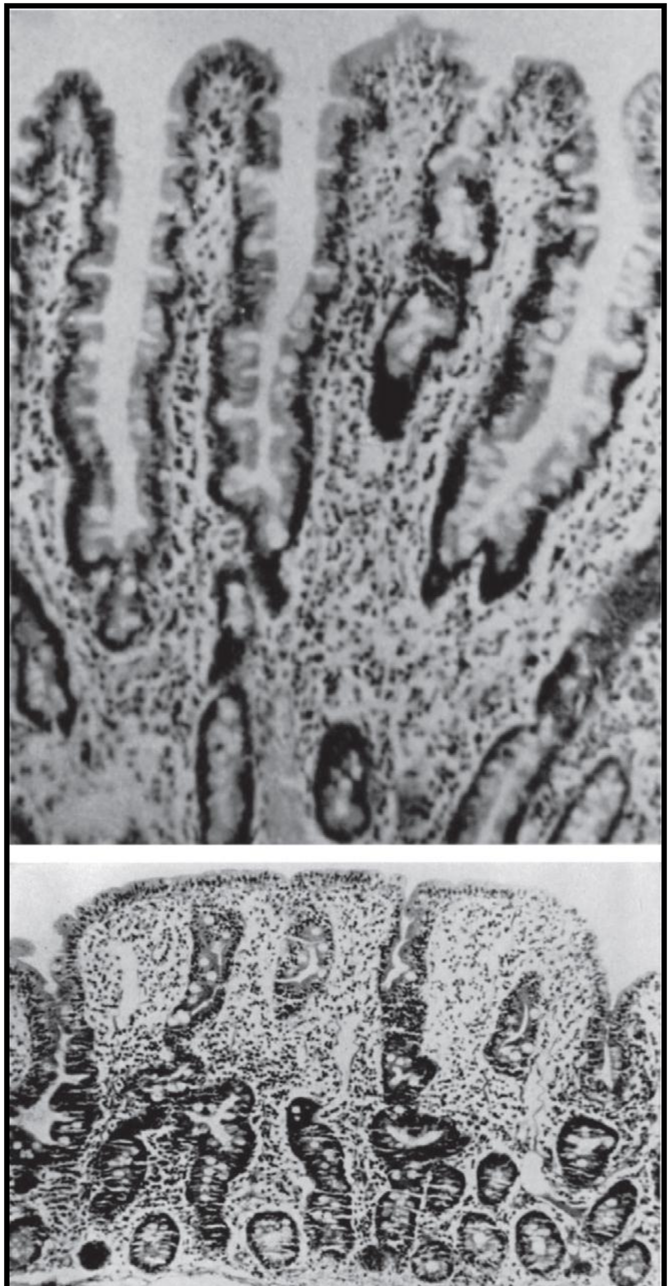
	Number of studies	Relative risk (95% CI)
Hygiene	11	0·63 (0·52–0·77)
Excluding poor quality studies	8	0·55 (0·40–0·75)
Handwashing	5	0·56 (0·33–0·93)
Education	6	0·72 (0·63–0·83)
Sanitation	2	0·68 (0·53–0·87)
Water supply	6	0·75 (0·62–0·91)
Diarrhoea only	4	1·03 (0·73–1·46)
Household connection	2	0·90 (0·43–1·93)
Standpipe or community connection	3	0·94 (0·65–1·35)
Water quality	15	0·69 (0·53–0·89)
Source treatment only	3	0·89 (0·42–1·90)
Household treatment only	12	0·65 (0·48–0·88)
Household treatment		
• excluding poor quality studies	8	0·61 (0·46–0·81)
• rural location	6	0·61 (0·39–0·94)
• urban/periurban locations	5	0·86 (0·57–1·28)
• urban/periurban excluding Sathe[35]	4	0·74 (0·65–0·85)
Multiple	5	0·67 (0·59–0·76)




Child has Diarrhea:
1. Treat Child To Prevent Death, Morbidity
2. To Prevent Diarrhea: Add Water and Sanitation

… focus moves to enteropathy

- 1970s: “tropical enteropathy” was identified in South and Southeast Asia, Africa
- Characterized by blunted intestinal villi, ↑ intestinal permeability; fat and carbohydrate malabsorption, and increased protein needs.
- Found in both children and adults
- Realization it was epidemiologically linked to living in an **unsanitary environment**



ENVIRONMENTAL ENTEROPATHY (EE)

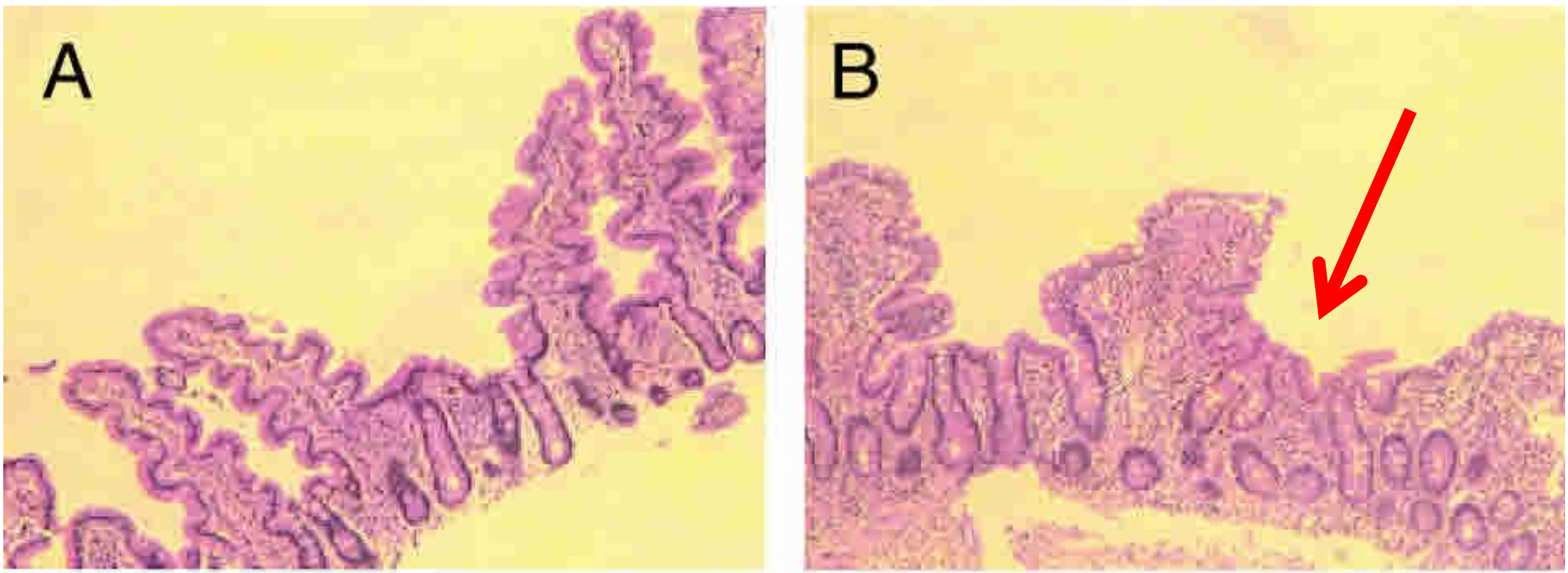
- People living in contaminated environments have leaky, chronically inflamed intestines
- Gut: short blunted villi, tissue infiltrated with inflammatory cells. Good evidence that gut contents, endotoxins 'leak' across the intestine.
- Associated with ↑ caloric, protein, carbohydrate needs

Korpe & Petri, Trends in Molecular Medicine June 2012, Vol. 18, No. 6

Am. J. Trop. Med. Hyg., 70(4), 2004, pp. 412–419

RESPONSES OF SMALL INTESTINAL ARCHITECTURE AND FUNCTION OVER TIME TO ENVIRONMENTAL FACTORS IN A TROPICAL POPULATION

PAUL KELLY, IAN MENZIES, ROGER CRANE, ISAAC ZULU, CAROLE NICKOLS, ROGER FEAKINS, JAMES MWANSA, VICTOR MUDENDA, MAX KATUBULUSHI, STEVE GREENWALD, AND MICHAEL FARTHING



Mild (left) and severe (right) villus blunting

Less absorptive surface area is present

Am. J. Trop. Med. Hyg., 70(4), 2004, pp. 412–419

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TABLE 4

Intestinal infections detected in 3,260 monthly samples from asymptomatic participants*

Organism	Frequency of isolation	Frequency of isolation one month before investigation
Cryptosporidium parvum	31	1
Isospora belli	11	0
Microsporidia	5	0
Giardia intestinalis	40	5
Blastocystis hominis	236	19
Ascaris lumbricoides	489	33
Hookworm	92	13
Strongyloides stercoralis	11	0
Schistosoma mansoni	12	0
Trichuris trichiura	6	0
Taenia saginata	7	0
Iodamoeba butschlii	120	5
Entamoeba histolytica/dispar	12	0
Entamoeba hartmannii	47	4
Chilomastix mesnili	208	25
Endolimax nana	259	12
Hymenolepis nana	19	2
Salmonella spp.	44	4
Shigella spp.	2	3
Aeromonas hydrophila	13	1
Citrobacter rodentium	608	42
Vibrio cholerae	3	0

* The table shows which organisms were isolated from asymptomatic participants and which organisms were isolated from participants in the month prior to investigations carried





Asymptomatic infection with gut pathogens

- Classic water, sanitation, hygiene (WASH) interventions reduce pathogen transmission;
- Tropical enteropathy → environmental enteropathy (EE) when the linkage to unsanitary environment recognized. Hallmark of EE is gut mucosal damage, permeability.
- Recognition that persons with EE have "asymptomatic" infections with pathogens

- Next question: how much of stunting can be explained by environmental enteropathy?

Lunn et al Lancet 1991: **Intestinal permeability, mucosal injury, and growth faltering in Gambian infants.**

- Infants aged 2-10 months recruited into longitudinal study (n=119 with at least 3 observations). Infants had diarrhea 7.5% of the time and "growth depressing permeability" 76% of the time. **43% of stunting** explained by increased gut permeability and decreased absorptive capacity (differential absorption of lactulose and mannitol) e.g. by E.E.

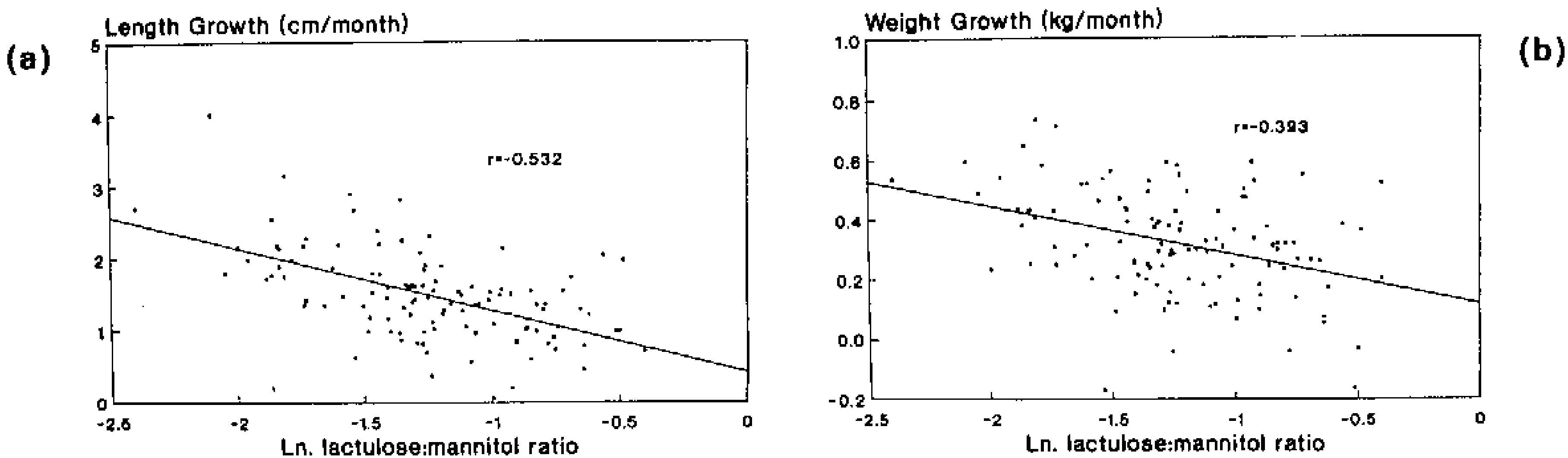
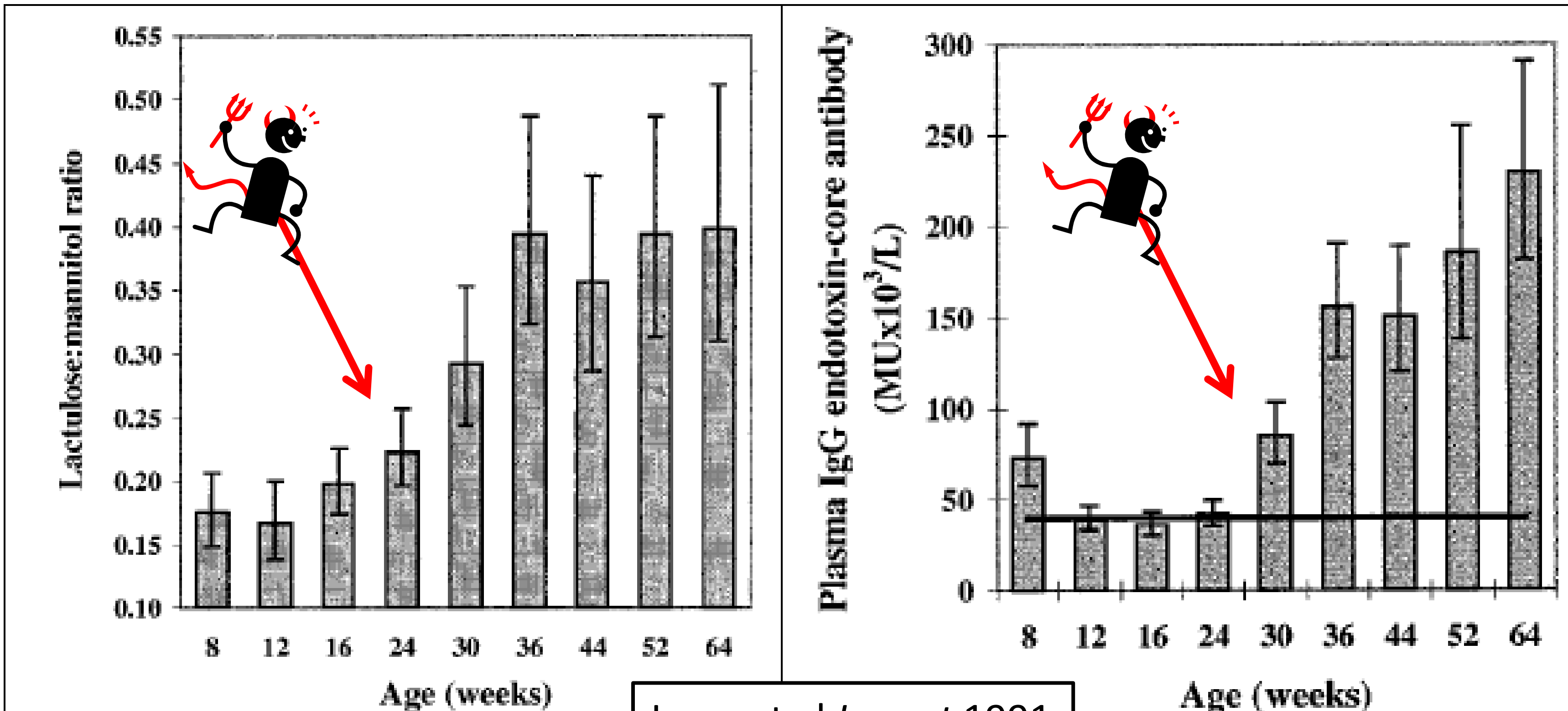


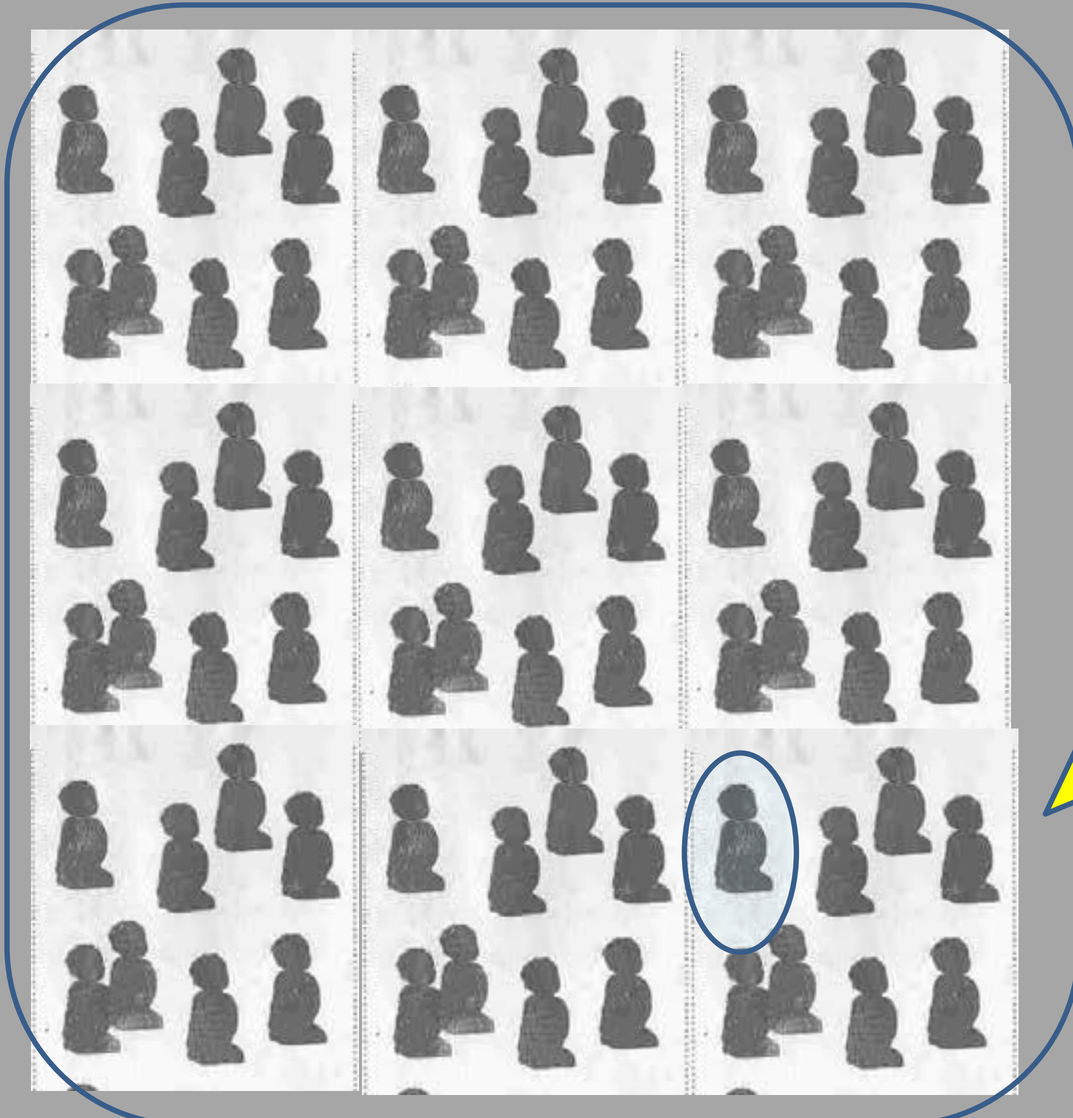
Fig 2—The relation between intestinal permeability (expressed as $\log_e$ lactulose:mannitol ratio) and mean monthly (a) length and (b) weight growth of 119 rural Gambian infants.

Significance of regression coefficients, $p < 0{\cdot}001$.

Intestinal permeability and mucosal damage (left) and antibody to bacterial endotoxin (right) rise after weaning when exposure to pathogens increases and nutritional faltering accelerates



Lunn et al *Lancet* 1991



REALITY:
All children at risk of Environmental Enteropathy, linked to Unsanitary Environment & Asymptomatic Infection with Pathogens

Handwashing is “necessary but not sufficient”

Amer J Human Biol 23:621-629 (**2011**)

Original Research Article

Hand-Washing, Subclinical Infections, and Growth: A Longitudinal Evaluation of an Intervention in Nepali Slums

REBECCA LANGFORD,[1*] PETER LUNN,[2] AND CATHERINE PANTER-BRICK[3]
[1]*School of Social and Community Medicine, University of Bristol, Canynge Hall, Bristol, BS8 2PS, United Kingdom*
[2]*Department of Biological Anthropology, University of Cambridge, Cambridge, CB2 3DZ, United Kingdom*
[3]*Jackson Institute for Global Affairs and Department of Anthropology, Yale University, New Haven, Connecticut*

- 1^{st} longitudinal study to assess hand-washing and enteropathy. 45 intervention, 43 control
- ↑enteropathy = ↓ growth ($p \leq 0.01$ HAZ, WAZ)
- **Handwashing led to 41% ↓ diarrhea morbidity**
- ***No* change in markers of enteropathy**
- *HW alone* doesn’t address chronic subclinical infxn

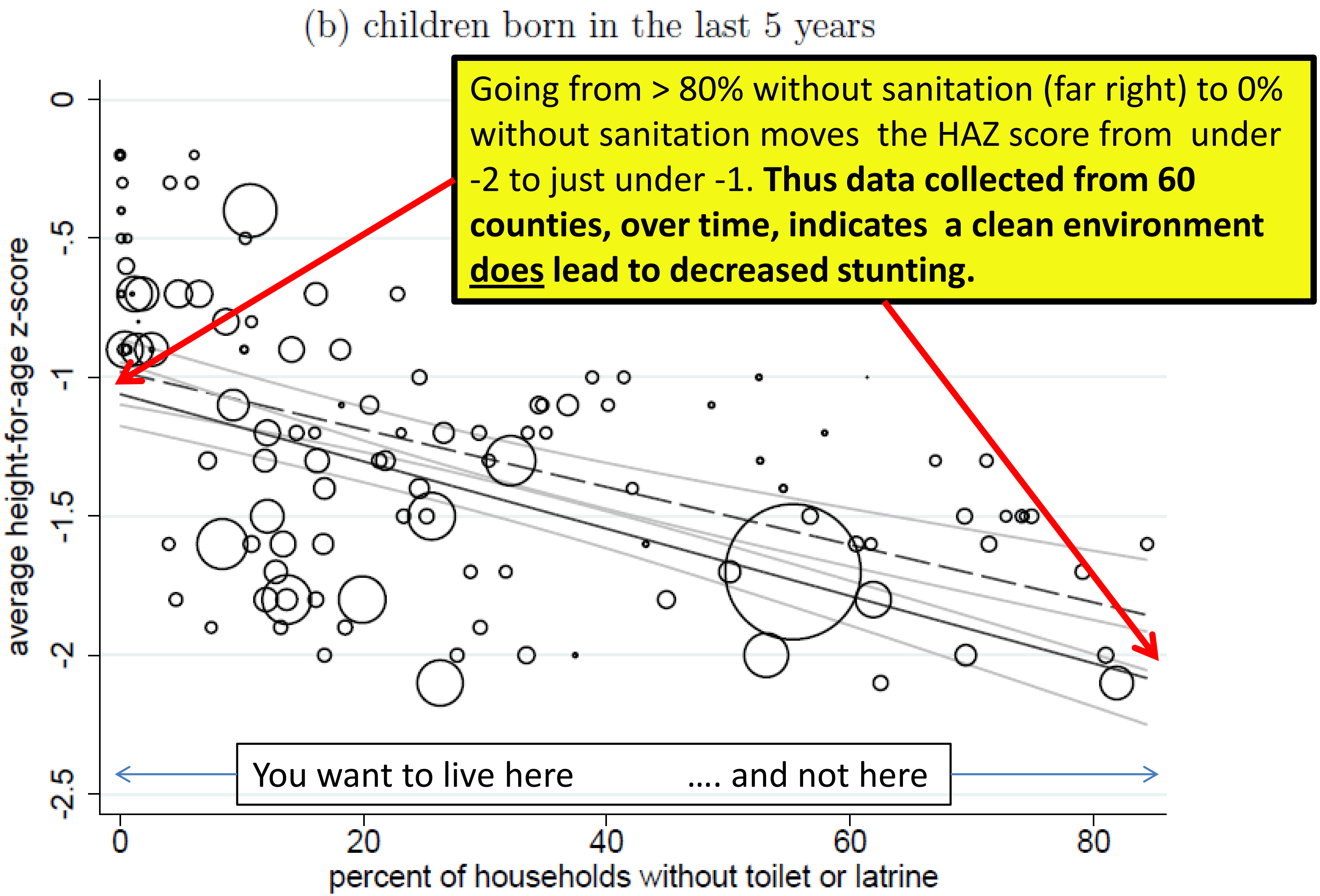


Figure 1: Open defecation predicts child height, across DHS survey round country-years

Solid OLS regression lines weight by country population; dashed lines are unweighted.

Key findings Spear's analysis of 140 DHS from 65 'developing' countries

- Open defecation (a certain marker of a fecally "contaminated environment") is linked to a **1.24 S.D. decrease** in the height of children.
- **This alone** accounts for **54%** of the between-country height variation (next slide).
- Open defecation and a lack of sanitation in an household, along with country GDP, predict child height *more than* mother's height or education; governance; or infrastructure.

Enteropathy & Nutrition

- Environmental enteropathy: malabsorption, permeable and chronically inflamed gut; infection with pathogens due to unsanitary environment (“bad microbiome”) AND
- Increased metabolic needs because of chronic intestinal inflammation and less absorption (↑ need for calories, carbos, fats, proteins…)
- Onset: weaning – when contaminated food and water lead to increased infections

How much international variation in child height can sanitation explain?

Dean Spears*

First circulated: 10 December 2012
This version: 17 January 2013

World Bank, 2013

EE goes away when a contaminated environment is removed. US Peace Corps volunteers develop EE when they live in rural African villages. When they return to the US, their EE goes away. **The absence of fecal material – be it human or animal – in the environment both prevents and "treats" EE. <u>Water/sanitation is critical to this separation</u>.**

- Dean Spears has looked at <u>open defecation</u> as a marker of <u>sanitation</u> using 140 DHS data sets from 60 countries.

How much stunting is due to poor sanitation?

Water is used for multiple purposes

- Agriculture / Irrigation
- Food, Cooking
- Industrial uses
- Support farm animals
- Recreation
- Worship
- Aquaculture and Fisheries


FAO

High potential for animals and people to contaminate household environment and water with feces

AGRICULTURAL WASTEWATER

ORGANISM	TYPICAL SOURCE
ROTAVIRUS	HUMANS; PERHAPS ZOONOTIC
HEPATITIS A	HUMANS
HEPATITIS E	HUMANS, SWINE
E. coli (bacteria)	CATTLE, HUMANS
Shigella species	HUMANS
Salmonella enterica (bacteria)	CATTLE, POULTRY, SWINE, HUMANS
Campylobacter jejuni (bacteria)	POULTRY
*Cryptosporidium** (protozoan)	CATTLE, HUMANS, OTHER FARM ANIMALS
*Microsporidia** (fungus)	FARM AND DOMESTIC ANIMALS, HUMANS

* Causes chronic diarrhea, wasting, malnutrition in people with HIV/AIDS

Cryptosporidium – a leading cause of diarrhea children < 24 months; known to cause stunting; and African children have x 4 risk of death in next year

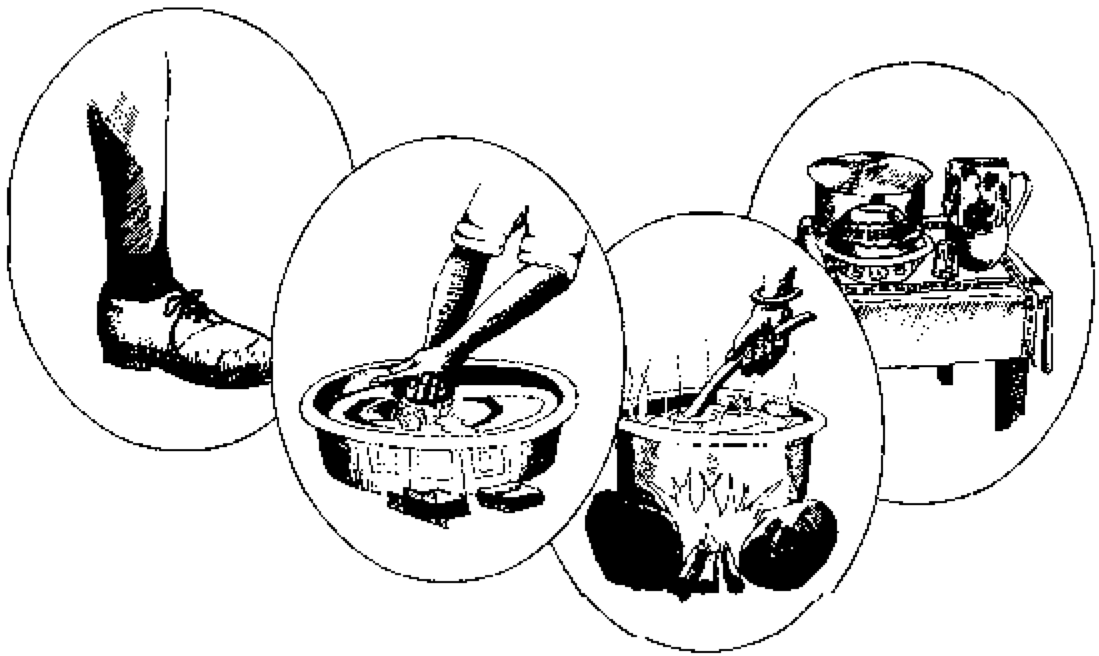
Pathogens in Rural and Agricultural Water and Watersheds. USDA 2010

Solutions

- **Classic water and sanitation for household** – water supply NOT same for animals unless treated; hand-washing; human feces kept out of wastewater
- **Agricultural hygiene** – barriers to keep feces and crud out of water - vegetated buffer zones around crops, riparian buffers to slow entry into open water (stream or irrigation canal), manure management, grazing practices …

January 4 2013: FDA proposes rules to “ensure water used in irrigation meets standards…”

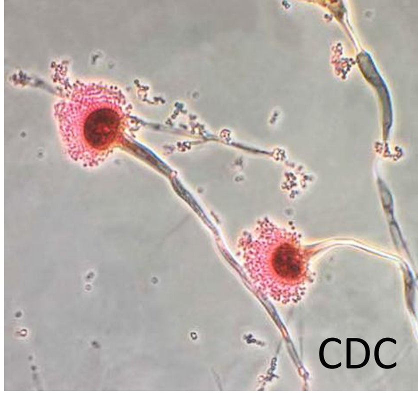
Farm practices to control spread of disease are well known



PHAST Step-by-Step Guide: A Participatory Approach for the Control of Diarrhoeal Disease (SIDA - UNDP - WB - WHO, 1998, 124 p.)

Aflatoxins and other mycotoxins

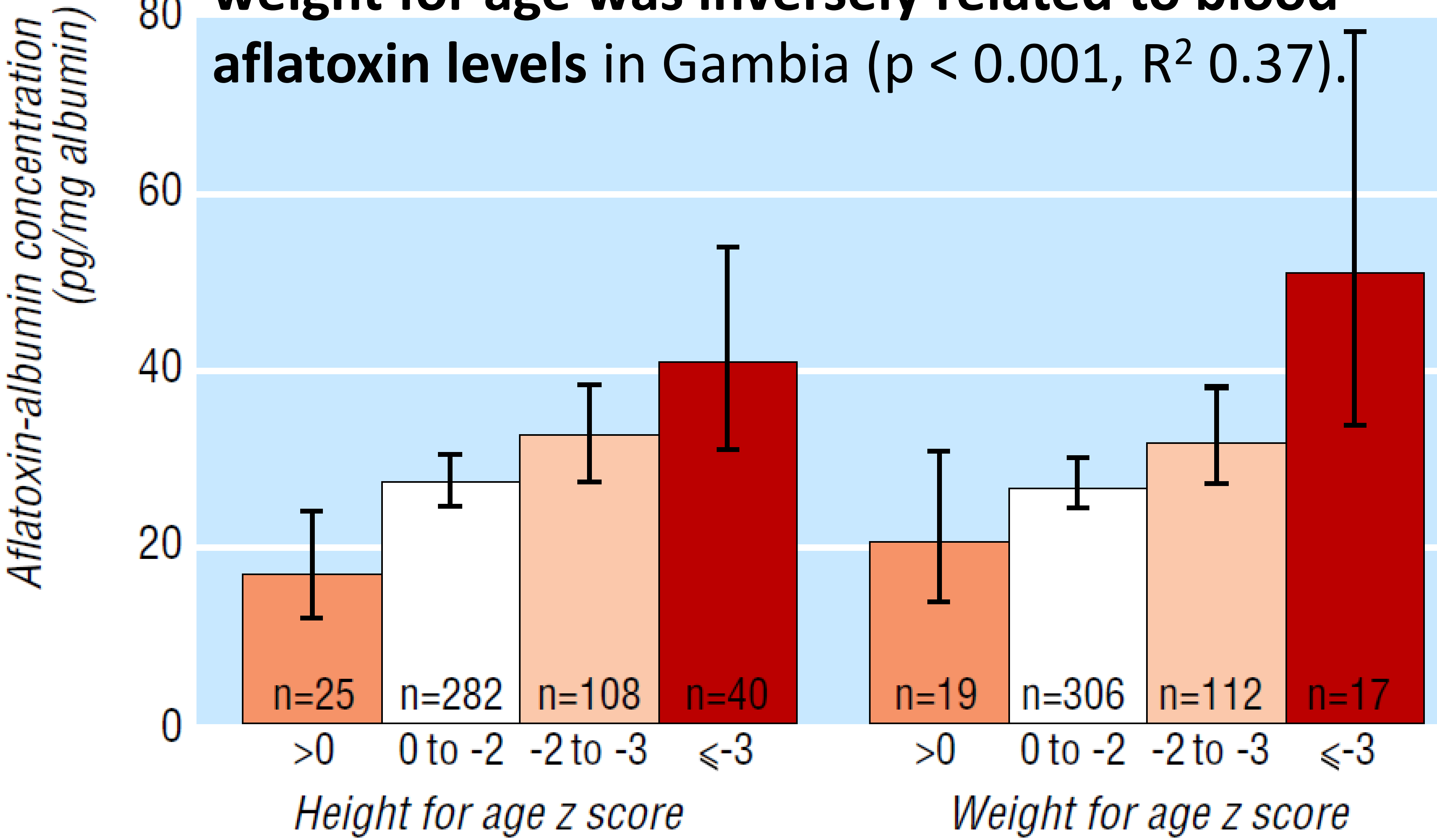
Aflatoxins (aflatoxins are a subset of mycotoxins)



- Produced by *Aspergillus* fungus
- Known – hepatoxic & cause liver cancer in people
- Known in mammals to cause growth faltering and ↓ *in utero* growth (e.g. low birth weight)
- Associated* with lower birth weight, growth, stunting, and wasting in children
- Associated* with lower CD4 and higher viral loads (e.g. worse immunity) in people with HIV
- Widespread exposure in sub-Saharan Africa, SE Asia; maize, peanuts, many other crops.

*Some criticize these studies for only being "associative" - but it is *unethical* to give aflatoxins to people. Prospective studies of exposure and outcomes are needed to show "causation."

Gong et al (BMJ, 2002) showed that **stunting** and **weight for age was inversely related to blood aflatoxin levels** in Gambia ($p < 0.001$, R^2 0.37).

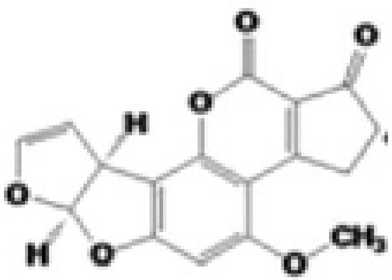


Cassava being dried on the ground: note green/yellow fungal discoloration

Photo: J K Griffiths Kamwenge, Uganda December 2012

Aflatoxins II

- Contamination occurs in the field; promoted by poor post-harvest storage (excess moisture).
- Passed *in utero* and in breast milk to children
- Complementary foods (e.g. baby foods such as porridge made from maize) is frequently contaminated – as are milk, eggs, chickens, animal meats…
- Note: in foods introduced when infants are weaned



Ingested Aflatoxin Inhibits Protein Synthesis Found in Staple Foods; Breast Milk; Dairy and Poultry; not Destroyed by Cooking

Impaired Tight Junctions

Reduced Barrier Function
Leakage of Gut Contents

Inhibition of Gut Regeneration

Altered Intestinal Architecture

Systemic Immune Activation

Glucose /Galactose Malabsortion

This looks like environmental enteropathy!

GROWTH FALTERING

Adapted from Smith, Stoltfuz, Prendergast, Food Chain Mycotoxin Exposure, and Impaired Growth: A Conceptual Framework *Advances Nutr*2012; 3:526

Poor populations:

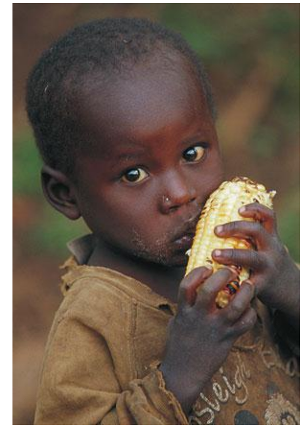
-Will likely eat aflatoxins in foods

-Many will have environmental enteropathy and live without good water or sanitation

-Lacking WASH and barriers to fecal contamination, they will have a different spectrum of gut bacteria than people with good WASH


Maize, groundnuts
Key staple crops

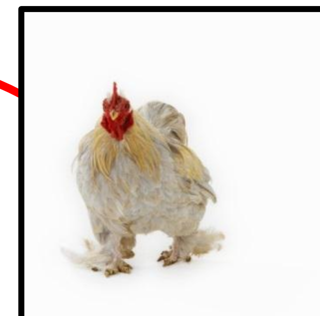
Aspergillus spp. + moisture + warm temperature = Aflatoxin formation



Aflatoxin ingestion, duodenal uptake - Metabolites bind to DNA, proteins – can measure in blood, urine, tissues
Immunosuppression

Agricultural interventions

Leaky Inflamed Intestine (EE)



Enteropathy – permeable intestine with documented increased nutrient needs, state of chronic inflammation
Microbiome – less diverse, abnormal nutrient utilization by flora

WASH interventions

Nutrition interventions

Clinical Manifestations:
Cycle of repeated infections
Worsening nutritional status – stunting, underweight, IUGR

Diet, Societal Conditions
Diet: poor diversity, inadequate caloric & micronutrient intake, leading to **immunosuppression**
Pathogen exposure: Widespread food, water, environment contamination

Take-Home: healthy growth requires:

- Adequate, varied nutrition with enough calories, micronutrients, and vitamins
- The absence of environmental toxins such as aflatoxins
- A clean environment which prevents environmental enteropathy, with its chronic inflammation and higher nutritional needs
- A normal gut microbiome which does not starve its host of nutrients and promote weight loss

Thanks!

Questions: jeffrey.griffiths @ tufts.edu

Photo: JK Griffiths Tanzania 2008