Vitamin A and Zinc

Saurabh Mehta, M.B.B.S., Sc.D.

Assistant Professor of Global Health and Nutrition
Division of Nutritional Sciences
Cornell University

September 27, 2011

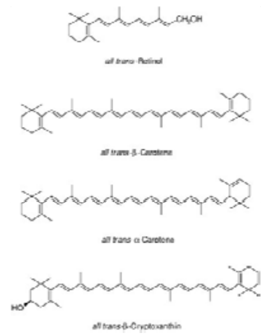
Vitamin A - History

- Sir Frederick Gowland Hopkins discovered that milk prevented death among rats fed purified diets (fat, starch, salts, and purified milk proteins)
  - *Fat-soluble A*
  - *What other nutrient was in Fat-soluble A?*
  - *World War I: Butter, an important source of fat-soluble A, scarce*
  - *Nobel Prize 1929 (with Christiaan Eijkman)*
- McCollum and Davis extracted "Vitamin A" from butter, egg yolk and cod liver oil

Hopkins, Sir Frederick Gowland. Photograph. Encyclopedia Britannica Online. Web. 26 Sep. 2011.

Vitamin A – Forms & Measurement

- Forms
  - Animal sources - Preformed vitamin A
    - Retinol, retinal
  - Plant sources - Carotenoids
    - *accessory pigments - ~600 - only 50 are pro-vitamin A*
- Measurement
  - Retinol Activity Equivalent (RAE)
    - 1 RAE = 1 µg Retinol
    - 1 µg beta-carotene = 1/2 RE if dissolved in oil; 1/12 RE if in the diet



Vitamin A | *Structure*

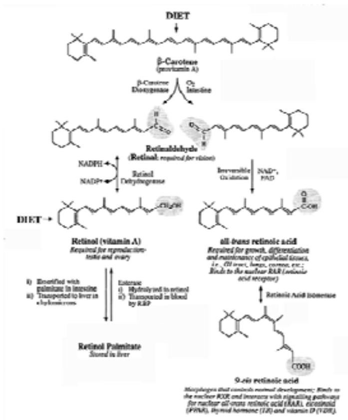
The National Academies Press. http://www.nap.edu/openbook.php?record_id=10026&page=84

Dietary Reference Intake

- Adults
  - Males: 900 µg/day
  - Females: 700 µg/day
    - Pregnancy: +70 µg/day
    - Lactation: +600 µg/day

Vitamin A – Common Sources

- Sources
  - Liver, fish oils (cod liver oil), organ meats
    - *~6500 µg in liver*
  - Cream, butter, fortified milks
    - *684 µg in butter; 265 µg in cheddar cheese*
  - Tropical fruits, carrots, sweet potatoes
    - *835 µg in carrots; 709 µg in sweet potato; 38 µg in mango*
  - Breast milk
  - Supplements



http://chemistry.gravitywaves.com/CHE452/images/ChemVitaminA.gif

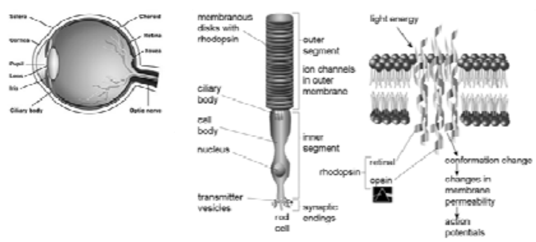
Vitamin A - Absorption

- Retinol & Carotenoids easily absorbed in the presence of fat
  - carried in chylomicrons
  - stored in liver as retinyl esters
  - retinol transported in plasma bound to RBP
- Absorption enhanced with increased dietary fat
- Excess intake stored in the liver
  - *Developed countries - 200-300 μg/g*
  - *Less-developed countries - <40 μg/g*

Vitamin A - Functions

- Functions
  - Vision - retinal comprises Rhodopsin

Vitamin A: Rhodopsin



Vitamin A - Functions

- Functions
  - Vision - retinal comprises Rhodopsin
  - Changes in Gene expression and transcription
    - Epithelial differentiation
    - Structural proteins - *Skin keratins*
    - Enzymes - *Alcohol Dehydrogenase*
    - Growth (Bone remodeling)
    - Reproduction
    - Apoptosis

Vitamin A and Embryonic Development

- Development of structures posterior to the hindbrain
  - *Vertebrae and spinal cord*
- Development of the limbs, heart, eyes, and ears
- Excess is teratogenic

Vitamin A and Immunity

- Innate Immunity
  - Maintenance of Epithelial Integrity
  - Acute phase response - increase in serum amyloid A and C-reactive protein
  - Enhanced monocyte differentiation and function
  - Increased cytotoxicity of natural killer cells
  - Improved neutrophil function
- Adaptive Immunity
  - Increase in T-cell counts, particularly CD4 cells
  - Increase in the antibody response to vaccines - tetanus toxoid and measles

Coutsoudis et al., 1992; Ross and Stephensen, 1996; Semba, 1998; Semba et al., 1992

Assessment of Vitamin A Status

- Clinical Signs
  - *Xerophthalmia*
- Functional
  - *Night blindness*
- Serum Retinol

Tanumihardjo S A Am J Clin Nutr 2011;94:658S-665S

Serum Retinol & Vitamin A Deficiency

- Prevalence among children > 1 year of levels ≤ 0.7 μmol/L
- Limitations: Acute Phase Reaction

Acute Phase Reaction

- Response to injury or inflammation
- Acute Phase Proteins
  - Positive - Plasma concentrations increase
    - *C-Reactive Protein (CRP)*
  - Negative - Plasma concentrations decrease
    - *Albumin, Retinol-binding Protein (RBP)*

Assessment of Vitamin A Status

- Clinical Signs
  - *Xerophthalmia*
- Functional
  - *Night blindness*
- Serum Retinol
  - *Not ideal in infection/inflammation*
- Dose Response

Tanumihardjo S A Am J Clin Nutr 2011;94:658S-665S

Relative Dose Response

- After fasting blood (A0), 600 μg retinol
- Breakfast
- 5 hours later second blood sample (A5)
- RDR= A5-A0/A5x100
- Vitamin A deficiency: RDR > 20%
- Public health problem if abnormal RDR:
  - mild < 20%; moderate 20-30%; severe >30%
- Limitation: Invasive

Modified Relative Dose Response

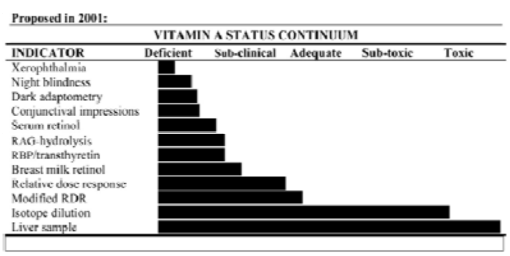
- Fasting dose of 1.5 mg of 3,4-didehydroretinol analog
- Single blood sample 4-6 hours later
- MRDR= 3,4-didehydroretinol/retinol
- Vitamin A deficiency MRDR ≥ 0.06
- Public health problem abnormal MRDR
  - mild <20%; moderate 20-30; severe >30%

Assessment of Vitamin A Status

- Clinical Signs
  - *Xerophthalmia*
- Functional
  - *Night blindness*
- Serum Retinol
  - *Not ideal in infection/inflammation*
- Dose Response
- Retinol Isotope Dilution
  - *Most sensitive biomarker of liver reserves*

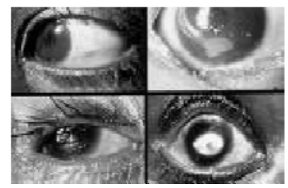
Tanumihardjo S A Am J Clin Nutr 2011;94:658S-665S

Biomarkers of vitamin A status relative to qualitative liver reserves of vitamin A.



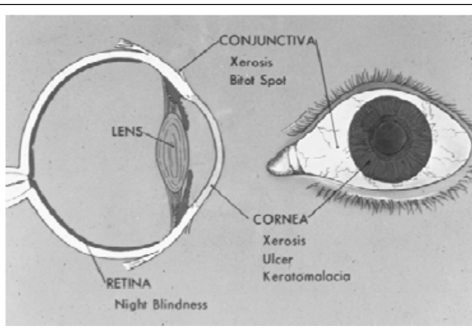
Tanumihardjo S A Am J Clin Nutr 2011;94:658S-665S

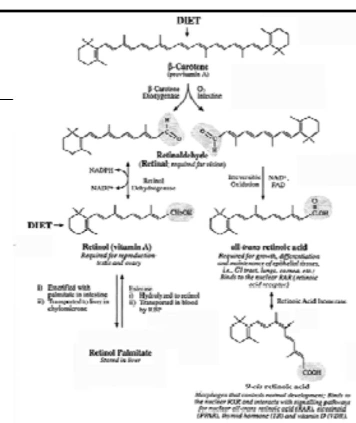
Deficiency



- Vision
  - Night blindness (rods)
  - Keratomalacia (epithelium)
  - Xerophthlamia

Vitamin A Deficiency: Eye Signs





http://chemistry.gravitywaves.com/CHE452/images/ChemVitaminA.gif

Deficiency

- Vision
  - Night blindness (rods)
  - Keratomalacia (epithelium)
  - Xerophthlamia
- Growth retardation
- Infections
  - *Increased number and severity*
- Child mortality

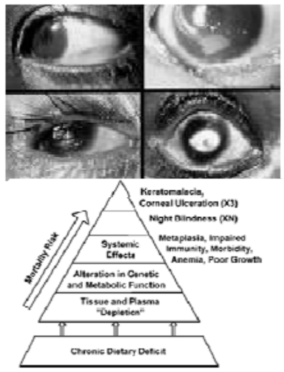


FIGURE 1 Spectrum of vitamin A deficiency disorders (VADD).

West KP, et al. J Nutr 2002;132:2857S-2866S

Public Health Problem

Criteria	***Prevalence in population at risk (6 months to 6 years)***
Nightblindness	>1%
Bitot's spots	>0.5%
Corneal Xerosis/Corneal Ulceration/Keratomalacia	>0.01%
Corneal Scarring	>0.05%
Serum Retinol (≤0.70 μmol/L)	>20%; 10-19%; 2-9%

http://www.who.int/vmnis/indicators/retinol.pdf

Global Perspective

Vitamin A Deficiency - Magnitude

- Vulnerable groups
  - Pregnant women
  - Children
    - *During periods of rapid growth*
- More than half the countries in the world affected
  - *Areas with high infectious disease burden*
- 250 million preschool children
- 250,000-500,000 vitamin A-deficient children become blind every year
  - 50% of these children die within 12 months of losing their sight

World Health Organization

Vitamin A Deficiency | *Based on serum retinol*

World Health Organization

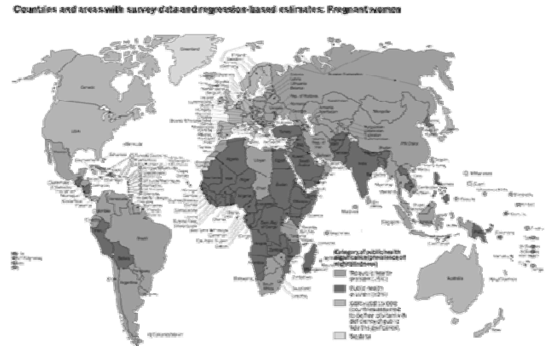
Vitamin A Deficiency | *Night Blindness*

World Health Organization

Vitamin A Deficiency

Based on serum retinol

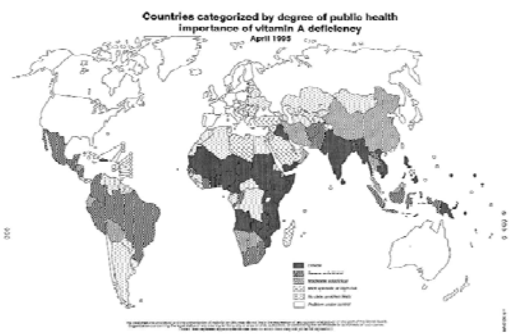
World Health Organization



Vitamin A Deficiency

Night Blindness

World Health Organization



Global Vitamin A Deficiency

World Health Organization

Vitamin A and Childhood Mortality

Vitamin A and Childhood Mortality

- Early 1980s: observational studies in Indonesia (Sommer) - children with xerophthalmia were more likely to die, compared to children without xeropthalmia
- Large community trial in Aceh, Indonesia (Sommer) - children (16 mo.) who received vitamin A supplementation every 6 months were significantly less likely to die, compared to those who did not receive vitamin A

Sommer, 1983; Sommer, 1986

Vitamin A and Childhood Mortality - Preschool

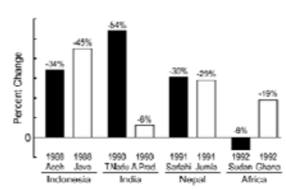


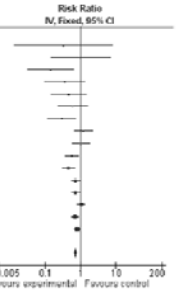
FIGURE 1 Impact of vitamin A on mortality. Relative mortality among children 6 mo–5 y of age randomized to receive periodic large-dose vitamin A supplementation. Eight major randomized clinical trials, 6 in Asia and 2 in Africa, randomized rural children to receive periodic vitamin A supplements at regular intervals. Six of the trials observed clinically and statistically significant reductions in mortality, 19–54%, compared with controls. Reproduced with permission (2).

Sommer A. J Nutr 2008;138:1835-1839

Figure 3. Forest plot of comparison: 1 Vitamin A versus Control, outcome: 1.1 Mortality (all-cause) at Longest Follow-up.

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
Lin 2008	0	0		Not estimable
Dibley 1994	-1.12232882	1.63299316	0.1%	0.33 [0.01, 7.99]
Barreto 1994	0	0.99838579	0.2%	1.00 [0.14, 7.08]
Chowdhury 2002	-1.94194975	0.75418055	0.4%	0.14 [0.03, 0.63]
Venkatarao 1996	-1.00252208	0.67056359	0.5%	0.37 [0.10, 1.37]
Benn 1997	-0.77629472	0.59367542	0.7%	0.46 [0.14, 1.47]
Donnen 1998	-0.51082562	0.48464603	1.0%	0.60 [0.23, 1.55]
Ross 1993 HEALTH	-1.21570729	0.46547467	1.1%	0.30 [0.12, 0.74]
Agarwal 1995	0.19717994	0.31200317	2.5%	1.22 [0.66, 2.25]
Vijayaraghavan 1990	0.01685569	0.2971801	2.7%	1.02 [0.57, 1.82]
Pant 1996	-0.56211092	0.222204	4.9%	0.57 [0.37, 0.88]
Rahmathullah 1990	-0.77652879	0.21976998	5.0%	0.46 [0.30, 0.71]
Sommer 1986	-0.30788478	0.15482032	10.1%	0.73 [0.54, 1.00]
Daulaire 1992	-0.30110509	0.14994833	10.7%	0.74 [0.55, 0.99]
Herrera 1992	0.05826891	0.13093651	14.1%	1.06 [0.82, 1.37]
West 1991	-0.35667494	0.11530445	18.1%	0.70 [0.56, 0.88]
Ross 1993 SURVIVAL	-0.21072103	0.09323125	27.8%	0.81 [0.67, 0.97]
Total (95% CI)			**100.0%**	**0.76 [0.69, 0.83]**

Heterogeneity: Chi² = 29.10, df = 15 (P = 0.02); I² = 48%
Test for overall effect: Z = 5.66 (P < 0.00001)



Imdad A, et al. Cochrane Database of Systematic Reviews 2010;12

Vitamin A and Childhood Mortality

- Led to substantial investments in research, and implementation of periodic vitamin A supplementation to children in 170 countries ($0.02 US $/dose)
- Issues
  - Timing
  - Dosage

Vitamin A and Childhood Mortality - 2 wks to 6 mo

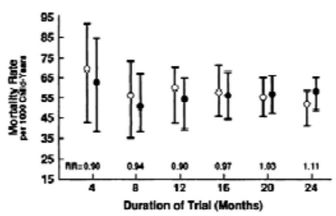
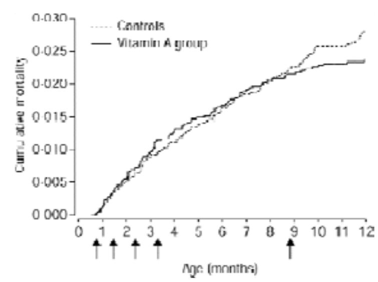


FIGURE 1. Cumulative mortality rate (with 95% CI) of infants < 6 mo of age at dosing by treatment group with duration of trial. (○) control, (●) vitamin A.

West KP, et al. Am J Clin Nutr 1995;62:143-148

Vitamin A and Childhood Mortality - 2 wks to 6 mo



WHO/CHD. Lancet 1998;352:1257-1263

Vitamin A and Neonatal Mortality

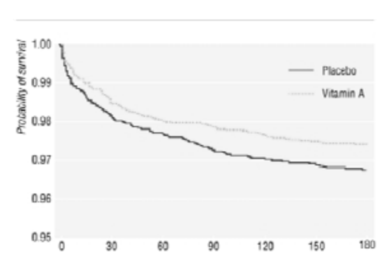
Table II. Mortality rate by gender and birth weight

	Control			Vitamin A			
	Death	Child-year	Death rate (per 1000 child-yr)	Death	Child-year	Death rate (per 1000 child-yr)	RR (95% CI)
Male							
<2500 gm	4	31.0	129.0	2	38.0	52.6	0.41 (0.08, 2.11)
≥2500 gm	9	461.1	19.5	0	467.8	0.0	0.05* (0.00, 0.95)†
All male	13	492.1	26.4	2	505.8	3.9	0.15* (0.03, 0.68)
Female							
<2500 gm	4	55.5	72.1	4	49.9	80.2	1.11 (0.29, 4.15)
≥2500 gm	2	409.5	4.9	1	414.0	2.4	0.50 (0.05, 5.56)
All female	6	465.0	12.9	5	463.9	10.8	0.84 (0.56, 2.77)
Both sexes							
<2500 gm	8	86.5	92.5	6	87.9	68.3	0.74 (0.26, 2.02)
≥2500 gm	11	870.6	12.6	1	881.8	1.1	0.09* (0.01, 0.70)
Total	19	957.1	19.8	7	969.6	7.2	0.36 (0.16-0.87)

*Groups differ; p less than 0.005 level.
†Relative risk calculated by assuming 0.5 death in vitamin A group.

Humphrey JH, et al. J Pediatr 1996;128:489-496

Vitamin A and Neonatal Mortality



Rahmathullah L, et al. BMJ 2003;327:254

Vitamin A and Maternal Mortality

Bangladesh

Table 3. Effects of Maternal Vitamin A or Beta Carotene Supplementation on All-Cause Mortality of Women Related to Pregnancy Through 12 Weeks of Age

	Placebo	Vitamin A	Beta Carotene
No. of pregnancies[a]	19862	19806	19998
No. of deaths[b]	41 (10, 8, 23)	47 (13, 11, 23)	50 (18, 15, 17)
Mortality rate (95% CI)[c]	206 (140-273)	237 (166-309)	250 (177-323)
Relative risk (95% CI)[d]	1 [Reference]	1.15 (0.75-1.76)	1.21 (0.81-1.81)
P value		.52	.35

West KP, et al. JAMA 2011;305:1986-1995

Bangladesh

Table 4. Effects of Maternal Vitamin A or Beta Carotene Supplementation on All-Cause— and Consensus-Cause—Specific Mortality of Infants Through 12 Weeks of Age

	Placebo	Vitamin A	Beta Carotene
All-cause mortality			
No. of live births[a]	13965	13898	14018
No. of deaths	951	904	979
Mortality rate (95% CI)[b]	68.1 (63.7-72.5)	65.0 (60.7-69.4)	69.8 (65.4-72.3)
Relative risk (95% CI)[c]	1 [Reference]	0.95 (0.87-1.05)	1.03 (0.94-1.12)
P value		.32	.58

West KP, et al. JAMA 2011;305:1986-1995

Ghana

	Placebo group	Vitamin A supplementation group
Woman-years of follow-up*	289 310	292 560
All-cause adult female deaths	1298	1326
Mortality rate (per 100 000 years)	449	453
Adjusted rate ratio† (95% CI)	1·00	1·01 (0·93–1·09)
p value	..	0·85

Data are number unless otherwise indicated. *Woman contributed after 6 months in consistent treatment group, and continued to contribute to that group for a further 2 months if she moved. †Rate ratio adjusted for clustering by use of random effects models.

Table 6: Effect of weekly vitamin A supplementation on all-cause female mortality (intention-to-treat analysis)

Kirkwood BR et al. Lancet 2010;375:1640-1649

Vitamin A and Maternal Mortality

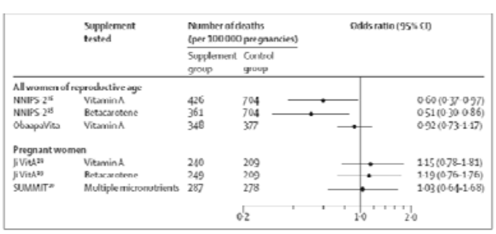
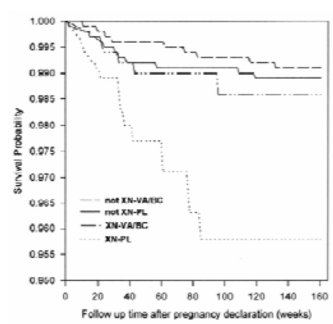


Figure 2: Effect of vitamin A supplementation on maternal mortality in cluster-randomised trials
NNIPS-2=Nepal Nutrition Intervention Project Sarlahi 2. SUMMIT=Supplementation with Multiple Micronutrients Intervention Trial.

Kirkwood BR et al. Lancet 2010;375:1640-1649

Survival of women by night blindness status during pregnancy and treatment allocation, Nepal, July 1994 to September 1997.



Christian P et al. Am. J. Epidemiol. 2000;152:542-547

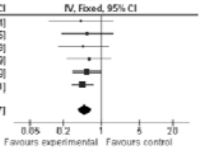
American Journal of EPIDEMIOLOGY

Vitamin A and Infections

Figure 7. Forest plot of comparison: 1 Vitamin A versus Control, outcome: 1.12 Measles Incidence at Longest Follow-up.

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Fixed, 95% CI
Bahl 1999	-0.84729786	0.68535975	4.9%	0.43 [0.11, 1.64]
Barreto 1994	-0.58778666	0.55487413	7.5%	0.56 [0.19, 1.65]
Bonn 1997	-0.75382186	0.53127063	8.2%	0.47 [0.17, 1.33]
Herrera 1992	-0.51082562	0.46579746	10.7%	0.60 [0.24, 1.49]
Semba 1995	-0.59969157	0.30298271	25.2%	0.55 [0.30, 0.99]
Chowdhury 2002	-0.79830607	0.2303533	43.6%	0.45 [0.29, 0.71]
Total (95% CI)			**100.0%**	**0.50 [0.37, 0.67]**

Heterogeneity: Chi² = 0.55, df = 5 (P = 0.99); I² = 0%
Test for overall effect: Z = 4.61 (P < 0.00001)



Imdad A, et al. Cochrane Database of Systematic Reviews 2010;12

Vitamin A Interventions

Crop Modification

- Biocassava Plus
  - 2nd most important source of calories in sub-Saharan Africa
  - #1 food crop -117 million tonnes in 2008

Table 2 Nutritional qualities of cassava foods (FAO). Cassava roots are a rich source of calories but do not provide complete nutrition

Cassava meal	Energy (kCal)	Protein (g)	Iron (mg)	Zinc (mg)	Vitamin E (mg)	Vitamin A (mg)
MDR (%)	~80	30	<30	<30	10	10
Boiled	740	5.5	2.0	2.0	1.0	5
Dry	1,775	10.5	4.0	4.0	1.0	15
Flour	1,710	7.5	4.0	3.0	1.0	9
Fresh	745	6.0	2.0	2.0	1.0	5
Roasted	1,360	10	2.5	3.0	1.0	5

Abbreviations: FAO, Food and Agricultural Organization; MDR, minimum daily requirement in a 500-g meal.

Sayre R, et al. Annu Rev Plant Biol 2011;62:251-272

Biocassava Plus

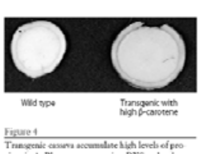


Figure 4
Transgenic cassava accumulate high levels of pro-vitamin A. Plants overexpressing DXS and *crtB* (*right*) have elevated β-carotene relative to wild-type roots (*left*) (132).

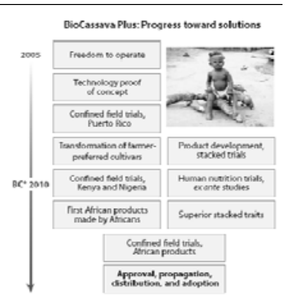
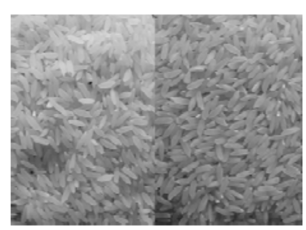


Figure 6
The BioCassava Plus (BC+) roadmap for product development and delivery.

Sayre R, et al. Annu Rev Plant Biol 2011;62:251-272

Golden Rice

- New improved variety
- A cup of golden rice can supply 50% of daily vitamin A requirement in rice-based societies



www.goldenrice.org
Tang G, et al. Am J Clin Nutr 2009;89:1776-1783

Vitamin A Supplementation

- Most common method
- Periodic supplementation after 6 months of age
  - 6-11 months: 100,000 IU
  - 12-60 months: 200,000 IU every 3-6 months

Vitamin A Summary

- Vitamin A deficiency is a major public health problem
- Supplementation in children after 6 months of age reduces morbidity and mortality; at birth, may reduce mortality
- No evidence of benefits of supplementation in mothers, who are not vitamin A deficient
- Role in infections - more in later classes

Zinc - History

- Syndrome of Dwarfism, Hypogonadism, and Anemia in Iran and Egypt
- First cases of human zinc deficiency

Biochemical Studies on Dwarfism, Hypogonadism, and Anemia

Introduction

Clinical Material and Methods

www.princemahidolaward.org

Zinc - Dietary Reference Intake

- Men: 11 mg
- Women: 8 mg
  - Pregnancy: 11 mg
  - Lactation: 12 mg

Zinc – Common Sources

- Dietary sources
  - Animal products: meat, seafood, milk
    - *Oysters: 76.7 mg per serving (6 medium)*
  - Cashews, Almonds
  - Baked beans, chickpeas, peas, kidney beans

Zinc Metabolism

- 10-40% absorbed in small intestine
  - *~25% absorbed from mixed diets*
- Absorption decreased by:
  - Iron
  - Phytate
  - Malabsorptive states
- Excreted in the stool
- No specific Zinc store
  - *needs to be consumed regularly*

Zinc - Functions

- Functions
  - Activating cofactor for 70 important enzyme systems
    - Carbonic anhydrase, dehydrogenases, carboxypeptidases
    - DNA and RNA Polymerase
  - Growth
  - Protects against lipid peroxidation; tissue repair/wound healing
  - Immune function
    - Reduced B- and T-cell function
    - Decreased phagocytosis and cytokine production

Shankar and Prasad. AJCN 1998; 68:447S.

Assessment of Zinc Status

- Plasma Zn
- Hair Zn levels
  - *Responsive to supplementation*
- Functional assays
  - Alkaline phosphatase
- High risk of deficiency at the population level
  - Prevalence of low plasma zinc concentration ≥ 20%
  - Prevalence of inadequate dietary intake of zinc ≥ 25%
  - Prevalence of stunting in under-five year olds ≥ 20%

Zinc Deficiency

- Syndrome of Dwarfism, Hypogonadism, and Anemia in Iran and Egypt
- Congenital Zinc deficiency/Acrodermatitis enteropathica
  - *Treatment: Lifelong Zinc supplements*
- Malabsorptive states
  - Crohn's disease
  - Celiac disease
  - Cystic fibrosis

Zinc Deficiency - Symptoms

- Deficiency symptoms
  - Growth failure
  - Primary hypogonadism
  - Skin disease - *skin ulcerations, alopecia*
  - Impaired taste/smell
  - Cognitive impairment
  - Impaired immunity - *recurrent infections*

Zinc and Growth

Trial in Paris

- 57 breastfed infants aged 4-9 months, many of African origin
- Randomization: 5 mg Zinc daily or Placebo
- Followed for 3 months

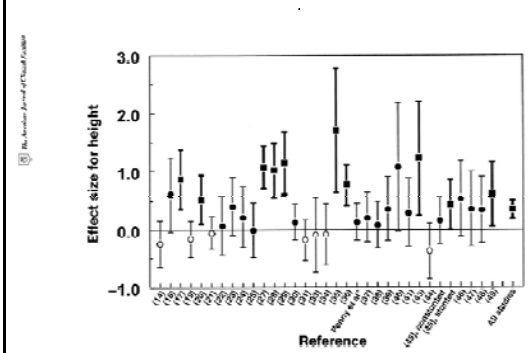
Walravens et al., Lancet 1992; 340:683

Zinc and Growth

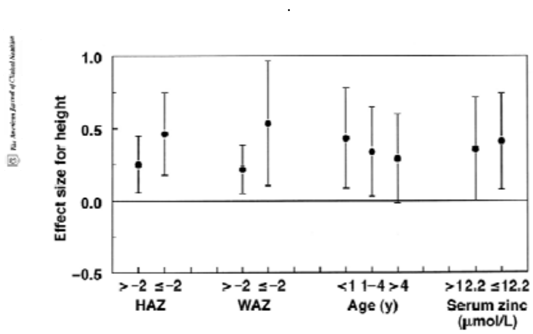
TABLE II—CHANGES IN WEIGHT, LENGTH, AND Z-SCORES FOR ZINC AND PLACEBO GROUPS

—	Mean (SEM)		p
	Zinc	Placebo	
Weight (kg)			
0–1 mo	0·56 (0·07)	0·44 (0·06)	0·303
0–2 mo	1·10 (0·09)	0·84 (0·07)	0·062
0–3 mo	1·64 (0·13)	1·26 (0·09)	0·047
Length (cm)			
0–1 mo	2·3 (0·3)	2·2 (0·3)	0·990
0–2 mo	4·3 (0·3)	3·7 (0·3)	0·256
0–3 mo	6·1 (0·3)	5·0 (0·3)	0·033
Weight-for-age Z-score			
0–1 mo	−0·02 (0·06)	−0·15 (0·06)	0·148
0–2 mo	−0·09 (0·08)	−0·27 (0·08)	0·098
0–3 mo	−0·06 (0·11)	−0·31 (0·09)	0·083
Length-for-age Z score			
0–1 mo	0·11 (0·10)	0·08 (0·12)	0·874
0–2 mo	0·18 (0·10)	−0·01 (0·10)	0·214
0–3 mo	0·21 (0·11)	−0·13 (0·10)	0·029

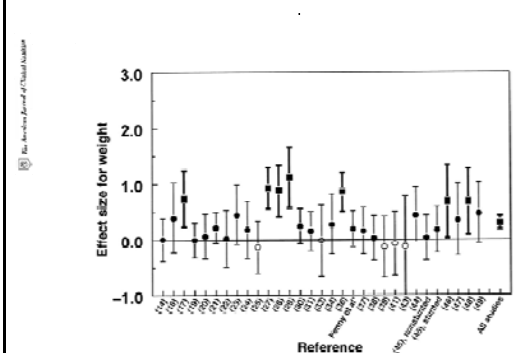
Walravens et al., Lancet 1992; 340:683



Brown K H et al. Am J Clin Nutr 2002;75:1062-1071



Brown K H et al. Am J Clin Nutr 2002;75:1062-1071



Brown K H et al. Am J Clin Nutr 2002;75:1062-1071

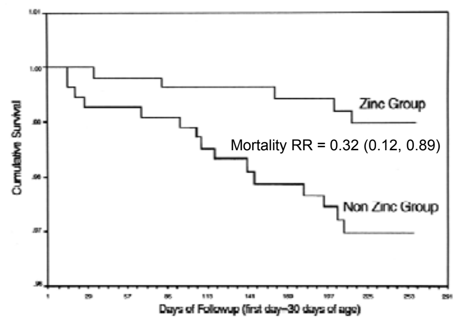
Zinc and Mortality

Zinc and Mortality

- RCT of 1154 full-term small-for-gestational age Indian infants randomized to:
  - Riboflavin
  - Riboflavin, Iron, folate, Ca, and P
  - Riboflavin and Zinc (5 mg)
  - Riboflavin, Zinc, Ca, P, folate, and Iron
- Daily dose between 30 and 284 days of age
- Household visits 6 times a week

Sazawal S et al. Pediatrics 2001;108:1280-1286

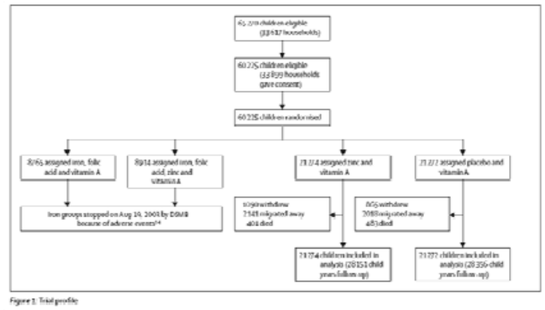
Survival curves for zinc-supplemented and non-zinc-supplemented groups.



Sazawal S et al. Pediatrics 2001;108:1280-1286

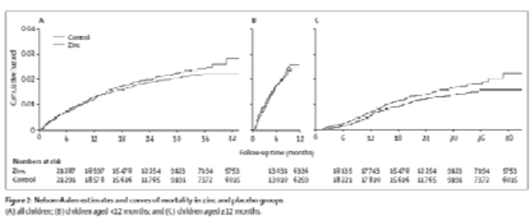
PEDIATRICS

Zinc and Mortality in Pemba



Sazawal S et al. Lancet 2007;369:927-934

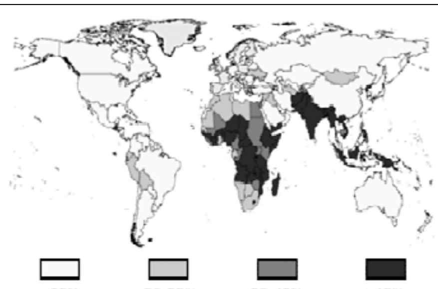
Zinc and Mortality in Pemba



Sazawal S et al. Lancet 2007;369:927-934

Global Perspective

Stunting as a Proxy for Zinc Deficiency



http://www.izincg.org/news/stunting

Populations at Risk

- Infants, Children, and Pregnant/Lactating Women
- Elderly
- Malabsorptive states

Zinc Interventions

Options

- Food Fortification
  - Prevention
  - Staple and constant food vehicle - *e.g. Wheat or corn flour for zinc*
  - Stable fortificant
  - Dose delivered should be adequate for beneficial effect but not toxic to those who already are zinc-replete - *Targeted?*
- Dietary diversification or Modification
  - Household interventions for improving zinc bioavailability include fermentation, germination, and soaking to remove phytates
- Supplementation

Zinc Summary

- Critical nutrient for child health and growth
  - More in the talk on Diarrhea and Respiratory Infections
- Extent of dietary insufficiency is not known globally
- Nor is the optimal method of improving zinc status....

Acknowledgments

- Christopher P. Duggan