

**Micronutrients for Health
Cooperative Agreement: 1997-2001**

**Center for Human Nutrition
Department of International Health
Johns Hopkins School of Public Health
Baltimore, MD**

**Annual Report: YEAR 1
FY 1998
(October 1997-September 1998)**

Submitted by:

**Keith P. West, Jr., Dr.P.H., Principal Investigator
Alfred Sommer, Co-Principal Investigator**

To:

**Office of Health and Nutrition
U.S. Agency for International Development
Washington, DC**

This report was prepared under Project Number 936-5122.05 and Contract Number HRN-A-00-97-00015 between the Center for Human Nutrition (CHN), The Johns Hopkins University, and the Office of Health and Nutrition, United States Agency for International Development.

Executive Summary

The Micronutrients for Health Cooperative Agreement (MHCA) is a collaborative applied research, technical assistance and training project between The Center for Human Nutrition at the Johns Hopkins School of Public Health (JHU) and the Office of Health and Nutrition at USAID. Its purpose is to provide global research leadership in, historically vitamin A (VA) deficiency control, but over the past decade has expanded to include the prevention of other key micronutrient deficiencies. The strategic goals and objectives of the MHCA are to advance micronutrient deficiency control through applied research aimed at protecting the health and survival of children (SO #3) and women of reproductive age (SO #2), reducing transmission of HIV/AIDS and other STDs (SO #4), and reducing the burden of re-emerging diseases (SO #5). This FY 1998 Annual Report covers the first year of a five-year project, from 1 October 97 through 30 September 98. It is a report on activities proposed in the original five-year agenda (dated May 1996), modified by a letter to USAID (dated 2 June 1997) and updated by integrating new knowledge and ongoing discussions within JHU and with colleagues at USAID on emerging micronutrient deficiency research priorities in this rapidly evolving area of public and international health and nutrition.

During FY 98 the JHU/MHCA team continued to focus on research to prevent vitamin A deficiency, in support of the Agency's "Vitamin A Enhanced Effort", while strengthening its research and adding considerably to knowledge on preventing iron deficiency, anemia and zinc deficiency in children and women. Significant progress was achieved in better understanding the ethnography and causality of key deficiencies, developing new indicators for assessment and approaches to prevention, quantifying the health and survival impact of micronutrient deficiency control among key target groups, especially among women and their newborn offspring, and in advocating, through global leadership and technical assistance, policies and programs toward prevention. JHU investigators maintained a diverse but coordinated stream of collaborative, applied, population-based research in a dozen countries throughout Asia, Africa and Latin America that we expect will continue to yield new findings that will help shape future micronutrient policies and programs and maintain USAID leadership in this vital area of health and nutrition. Several highlights illustrate these advances during FY 98:

New Findings

Vitamin A

- NNIPS-2 showed that supplementing Nepalese women with normal dietary amounts of vitamin A or beta-carotene could reduce maternal mortality by 40% or more. These findings and other findings were reported at the IVACG meeting in Cairo in late September 1997; featured in the UNICEF State of the World's Children Report and Video in December 1997, presented at the Experimental Biology '98 Meetings in San Francisco in April 1998, and submitted for publication (and subsequently accepted by the British Medical Journal).
- NNIPS-2 also showed significant improvements in vitamin A status, and reductions in maternal night blindness and anemia (the latter only in the relative absence of hookworm infection, clearly linking health and nutritional approaches).
- There was no impact of routine, low-dose maternal vitamin A or β -carotene supplementation on fetal or early infant mortality, suggesting that other interventions are required to improve infant survival through six months in non-HIV, chronically wasted populations.

- Seven publications and an IVACG Statement provided the basis for maternal night blindness (XN) to become recognized in FY 98 as a practical indicator of vitamin A deficiency and, more generally, poor nutritional status and high health and mortality risk of women. These NNIPS-2 findings also found application as a history of maternal XN began to be included in USAID/DHS and UNICEF/ MICS surveys during the year.
- In Bangladesh, findings on the efficacy of maternal post-partum vitamin A supplementation (200,000 IU) emerged, in meetings (IVACG, Sept 1998 & Experimental Biology '98) and publications (*J Nutr*, in press): High-potency dosing raised maternal vitamin A stores, but the effect waned after 6 months by which time infant vitamin A stores improved some. Daily β -carotene supplementation, on the other hand, slowly raised maternal vitamin A status over a 9-month period, but neither intervention fully corrected underlying vitamin A deficiency in mothers nor infants, suggesting that the currently recommended post-partum dosage of vitamin A be reconsidered.
- Results of a randomized, double-masked trial in Malawi, showed that maternal vitamin A supplementation of HIV+ can improve birth weight of their infants. But, while vitamin A deficiency is strongly associated with vertical transmission, maternal supplementation with vitamin A had no effect on the risk of transmitting HIV from mother-to-child. Other trials currently underway will provide the bases to confirm and explore new HIV-vitamin A/micronutrient relationships in several populations.
- Timely new studies and comprehensive reviews continued to provide clues that pregnant women with HIV/AIDS in Africa are afflicted with multiple micronutrient deficiencies which are likely to impair reproductive health.
- Findings from JHU trials among preschool children in Papua New Guinea began to be widely reported: One showed that 4-monthly vitamin A supplementation could reduce malaria attack rates by ~35% (provisionally accepted by the *Lancet*). A second, using zinc, also began to be reported (see below). The results have generated new hypotheses linking micronutrient status to the risk of malaria.
- Child care and feeding *behavioral* patterns in the household emerged in several papers as important factors that underlie chronic vitamin A deficiency in children: These include how frequently and with whom children share a plate at mealtimes, strong sibling care practices that propagate risk, aspects of household gardening and access to small animals.
- Blood spot retinol concentration, assessed by HPLC, is rapidly emerging as a potential indicator of vitamin A status based on collaborative work between JHU and Craft Technologies, Inc. A first paper relating this indicator to serum retinol concentration is under preparation.

Iron Deficiency and Anemia

- Published JHU studies from Tanzania reported on the effects of de-worming regimens and the roles of different hookworm species on iron status of children; in China on the relationship between gestational hemoglobin concentrations to birth outcome; in Peru on the effects of prenatal iron and zinc on hematological status of pregnant women.

- To assess maternal anemia and its correlates in the young infant, NNIPS-2 sub-study findings illustrated that regional causes of anemia should be understood, in terms of the roles of dietary iron deficiency, other micronutrient deficiencies, hookworm and malaria. Three papers are being prepared for publication.
- Long needed "Guidelines for the Use of Iron Supplements to Prevent and Treat Iron Deficiency Anemia" were prepared and published by JHU authors as a joint INACG/WHO/UNICEF report.

Zinc Deficiency

- The reduction of ~40% in malaria clinic attack rates and associated morbidity observed with daily zinc supplementation of preschool children during a second randomized field trial in PNG began to be disseminated (featured in the 1998 UNICEF SOWC Report, paper submitted for publication). The results of this study (and its sister vitamin A trial in PNG) has stimulated new interests in how micronutrient supplementation might lower the incidence or severity of malaria and other re-emerging infectious diseases (e.g., TB).
- Findings of improved maternal and neonatal zinc status and improved neurobehavioral development following maternal zinc supplementation in Peru began to be widely disseminated (5 papers published or in press during the year).

Research in Progress

- **Nepal:** NNIPS-2 field and data management activities were completed, while laboratory and data analysis continued; interim weekly dosing of women with vitamin A or β -carotene and vital event surveillance continued as prophylaxis; field work, laboratory and data analysis were completed for the maternal zinc treatment trial to assess efficacy in curing night blindness (co-funded by Nestle); field preparations got underway for beginning the NNIPS-3 multiple micronutrient maternal supplementation trial in Sarlahi District in FY 99 (co-funded by Roche).
- **India:** VASIN, the collaborative trial with the Aravind Children's Hospital in Madurai to assess the impact of dosing newborns with 50,000 IU vitamin A on infant mortality, began field work; Five Indian states were visited (Tamil Nadu, Gujarat, Andhra Pradesh, Madhya Pradesh and Orissa) to explore their potential as sites for a follow-up maternal mortality trial but none were selected.
- **Bangladesh:** Data analysis and reporting continued for the previous maternal post-partum vitamin A and β -carotene supplementation trial; A site visit was conducted and correspondence held throughout the year to explore Bangladesh as a site visit for a maternal mortality trial.
- **Thailand:** A collaborative trial with the Institute of Nutrition at Mahidol University continued to evaluate the effects of dietary intakes of a provitamin A-carotenoid rich diet on vitamin A body stores and status in lactating women (co-funded by the IAEA).
- **Papua New Guinea:** Laboratory analyses for the two vitamin A and zinc trials neared completion as efforts focused on definitive data analysis and preparing reports for publication.

- **Philippines:** Field work and data management were completed, and initial analysis and reporting done, for the randomized vitamin A-fortified *pandesal* trial (the trial and part of JHU effort was funded by OMNI).
- **Tanzania/Zanzibar:** Field and laboratory work and data management for the Schoolers Study, demonstrating the impact of de-worming on iron, growth and health status of school-aged children, was completed and several papers submitted for publication; "One Plus", a trial to assess the impact of iron supplementation on iron status and anemia risk in first graders, was launched toward the end of FY 98 (co-funded by WHO)
- **Zimbabwe:** "ZVITAMBO", a large collaborative trial with the ZMOH to assess the impact of postpartum maternal high-potency vitamin A supplementation on HIV mother-to-child transmission, infant mortality and maternal infection, was formally launched and enrolled nearly 6000 of its planned 12,000 pregnant women; the duration of postpartum follow-up was extended into a second year based on recommendations of an international data and safety monitoring committee (co-funded by CIDA).
- **Peru:** Data were analyzed and reports on birth and infant outcomes submitted for publication from the "Maternal Zinc Supplementation Trial-1" conducted in Lima; data collection began for the follow-up trial to assess the efficacy of a larger maternal supplement of zinc (25 vs. 15 mg) (co-funded by Nestle and USDA).
- **El Salvador:** A field trial is underway to assess the effect of VA supplementation on the response to two different formulations of Hi-B vaccines in infants. Findings from this study will help determine if VA supplementation of infants can enhance a child's H. influenza vaccine response.
- **Malawi:** Data were analyzed and reports were prepared on the impact of low-dose maternal VA supplementation during pregnancy on mother-to-child HIV transmission and birthweight.
- **Uganda:** A field trial to is in progress to determine the efficacy of VA as targeted therapy for reducing the progression of disease (as opposed to upregulating HIV, as some small studies have suggested) and survival in HIV-infected preschool (6-36 month old) children. Findings may help provide impetus for VA supplementation of HIV-infected infants (fieldwork fully funded under a NIH grant).

Technical Assistance and Advocacy

- Private partnerships in micronutrient deficiency prevention were strengthened as JHU facilitated new interactions between USAID and the food industry in support of the Agency's Enhanced Vitamin A Effort during the year.
- JHU-Roche collaboration reached new highs during the year: Roche initiated the endowment of a new "Sight and Life Institute" at JHU to conduct applied research to prevent maternal and child morbidity and mortality through general and micronutrient nutrition interventions; Roche produced through Jamieson Nutraceuticals in Canada and donated 1.5 million supplements to be used in the new NNIPS-3 trial that will test the efficacy of single and combined maternal micronutrient supplements on birth outcomes.

- JHU entered into an agreement with Monsanto Life Sciences Company to engage in research to test the efficacy and impact of new carotenoid-rich vegetable oils and other foods engineered to increase carotenoid and vitamin A content in the developing world.
- Visiting scholars from Indonesia and Morocco were assisted in preparing reports on studies in their respective countries.
- JHU/NNIPS was pleased to host Ms. Hattie Babbit, Deputy Administrator of the Agency, as she visited vitamin A programs and research projects in Nepal in the Spring of 1998.
- The CHN/JHU completed its technical assistance to OMNI and prepared itself to play a technical role under the new "MOST" CA, made possible because of expertise developed in the CHN under previous and the current CAs.

Core Activities

- Under the MHCA, JHU published ~60 peer-reviewed articles, book chapters or other reviews and 7 FASEB abstracts during FY 98. During the past two calendar years (1997 and 1998) over 76 CA-supported articles and 25 abstracts have appeared in the literature (see Appendices 2 and 3). A "steady stream" of articles appearing in lay reports such as the Sight and Life Newsletter, Nutriview, the UNICEF State of the World's Children's Report, etc helped to bring micronutrient research findings and their program relevance to policy makers.
- Data management capabilities were enhanced through the timely purchase of a new Sun server and CPU upgrade at JHU that will facilitate continued analysis of existing, major data sets from Indonesia, Nepal, India, the Philippines, Tanzania, Zimbabwe, Peru and other country studies for which data sets exist while accommodating data from planned studies during the next 4 years.
- In-house technical capabilities continued to improve to meet future challenges through in-depth training programs and CA-supported faculty taught a number of graduate school courses, attended by multinationals, that emphasize the control of vitamin A, iron, zinc and other micronutrient deficiencies.

Table of Contents

EXECUTIVE SUMMARY	ii
1. INTRODUCTION	1
2. MHCA COUNTRY PROGRAMS	2
2.1 Asia and Near East	3
Nepal	3
Bangladesh	6
India	6
Philippines	7
Thailand	7
2.2 Africa	7
Zimbabwe	8
Malawi	9
Uganda	10
Tanzania	10
Ghana	10
2.3 Latin America	11
El Salvador	11
Peru	11
2.4 Oceania	12
Papua New Guinea	12
3. NEW ASSESSMENT TECHNIQUES	12
4. CORE ACTIVITIES	14
4.1 Laboratory	14
4.2. Data Management and Analysis	15
4.3 Publications	15
4.4 Technical Assistance	15
4.5 Teaching	15
4.6 Advocacy	16
APPENDICES	1

List of Appendices

Appendix 1	Financial Summary
Appendix 2	1997 Publications (CY97)
Appendix 3	1998 Publications (Jan-Sept)
Appendix 4	Professional Services
Appendix 5	Lectures
Appendix 6	Meetings
Appendix 7	Technical Assistance
Appendix 8	Travel

1. Introduction

FY98 MHCA research, technical assistance and training/advocacy have focused on several priorities for specific micronutrients that can provide the required scientific evidence to advance the Agency's strategic child and maternal health and survival goals. Succinctly, these can be summarized as follows:

Vitamin A and Multiple Micronutrients

- Confirm the impact of maternal vitamin A supplementation, either preformed or as beta-carotene, in reducing pregnancy-related mortality and mortality due to severe infection.
- Evaluate the effects of supplementing women during pregnancy and lactation daily with multiple micronutrients on reproductive health outcomes, including fetal and early infant mortality, intrauterine and postnatal growth maternal, infant morbidity, and maternal night blindness, anemia, morbidity and mortality.
- Replicate and encourage further epidemiologic studies of maternal night blindness as a sensitive indicator of maternal and infant health risk.
- Evaluate the impact of maternal or newborn high-potency vitamin A supplementation on infant survival, vertical transmission of HIV, and maternal susceptibility to HIV infection and AIDS.
- Determine the effects of vitamin A supplementation on immune competence and resistance to emerging and reemerging infections, focusing on HIV/AIDS, malaria and tuberculosis, in women and children.
- Improve vitamin A status and dietary assessment with practical tools to determine prevalence, target groups at risk, monitor trends and evaluate program impact.
- Continue to identify behavioral determinants of poor dietary vitamin A intake to improve dietary intervention design, targeting and implementation.
- Increase availability of technical assistance for evaluating vitamin A programs to maximize coverage and impact.

Iron Deficiency and Anemia

- Reassess the definitions and public health significance of iron deficiency and anemia in children and women.
- Reveal the consequences of iron deficiency and anemia for child and maternal health and survival.

- Develop approaches to identify and assess the severity and importance of various causes of anemia as a public health problem in children and women that can provide a basis for programs and policies.
- Assess the impact of iron supplementation on cognition and learning of children.
- Evaluate the combined impact of anthelmintic and iron supplementation regimens on anemia.
- Explore the biological basis and public health importance of the interaction between vitamin A and iron with respect to anemia.

Zinc Deficiency

- Confirm findings on the impact of zinc supplementation in reducing the risk of malaria in children.
- Determine the effects of maternal antenatal zinc supplementation on maternal, fetal and infant health.
- Determine the role of zinc deficiency as a cause of maternal night blindness, and the efficacy of zinc supplementation in curing the condition in malnourished populations.
- Assess the impact of zinc supplementation, with or without iron supplements, in reducing preschool child mortality.

Iodine Deficiency

- Estimate, where feasible, the prevalence and associated risks of mild iodine deficiency in pregnant and lactating women.

2. MHCA Country Programs

During FY98 MHCA activities were carried out in different cultural settings in Asia, Africa and Latin America, specifically the following (Table 1).

Table 1. Countries in which MHCA-supported activities were undertaken during FY98

Asia	Africa	Latin America	Oceania
Nepal	Zimbabwe	El Salvador	Papua New Guinea
Bangladesh	Malawi	Peru	
India	Uganda		
Philippines	Tanzania/Zanzibar		
Thailand	Ghana		

2.1 Asia and Near East

Nepal

1. *NNIPS-2/Nepal*. This large randomized community trial in Sarlahi district examined the impact of low-dose weekly supplementation of women of child-bearing age with vitamin A, beta-carotene, and placebo, on maternal mortality and morbidity, fetal wastage, and early infant mortality. The trial supplemented over 44,000 women and enrolled over 22,000 pregnancies.

Accomplishments: Field work for NNIPS-2 was completed and data entry, management and data base definition activities were mostly completed. Women in the NNIPS study area continue to be supplemented with vitamin A (VA) or beta-carotene (BC) prophylactically for ethical purposes, and vital event surveillance continued while NNIPS-3 was being planned and the field site prepared. Data analysis and manuscript preparation for submission progressed regarding the impact of VA or BC supplementation on maternal mortality, fetal and infant mortality, maternal morbidity, iron deficiency, anemia and birth defects. Preliminary results were reported at the IVACG meeting in Cairo¹. The effects of supplementation on night blindness appeared in the *Journal of Nutrition* in August (Ref #3, Appendix 3). The paper describing supplement impact on maternal mortality was twice submitted to the *Lancet* but was rejected both times. It was subsequently submitted to the *British Medical Journal* and has been accepted.

2. *NNIPS-2 (Iodine add-on)*: This add-on study has allowed us to estimate the prevalence of iodine deficiency in pregnant and lactating women, examine risk factors and draw direct associations between iodine status and level of iodized salt use. As far as we know, these will be unique data for the plain populations of north-central South Asia and will generate data on the effectiveness of the existing salt iodization program.

Accomplishments: During NNIPS-2, urine samples were collected from pregnant and lactating women participating in the ~10% clinic sub-sample. These urine samples were archived, a urinalysis

¹ Christian P. West KP Jr, Katz J, Khatri SK, Kimbrough-Pradhan E, Shrestha SR, Pokhrel RP. The impact of vitamin A or beta-carotene supplementation on the incidence of night blindness during pregnancy and lactation in Nepal. XVIII IVACG Meeting, Cairo, Egypt 1997.

Dreyfuss ML, West KP Jr, Katz J, LeClerq SC, Pradhan EK, Adhikari RK, Stoltzfus RJ. Effects of maternal vitamin A or beta-carotene supplementation on intrauterine/neonatal and early infant growth in Nepal. XVIII IVACG Meeting, Cairo, 1997.

Khatri SK, LeClerq SC, Adhikari RK, Amatya R, Pradhan EK, Dreyfuss ML, Katz J, Wu LS-F, Shrestha JB, West KP Jr. Effect of maternal vitamin A or beta-carotene supplementation on incidence of birth defects among Nepalese infants. XVIII IVACG Meeting, Cairo, Egypt 1997.

LeClerq SC, West KP Jr, Katz J, Khatri SK, Pradhan EK, Shrestha SR, Connor PB, Sommer A. Purpose, design, and methods of a double-masked, randomized community trial on the impact of maternal vitamin A or beta-carotene supplementation in Nepal. XVIII IVACG Meeting, Cairo, Egypt 1997.

Rice AL, Stoltzfus RJ, de Francisco A, Chakraborty J, Kjolhede CL, Wahed MA. Maternal vitamin A or beta-carotene supplementation in lactating Bangladeshi women: effects on mothers and infants. XVIII IVACG Meeting, Cairo, 22-26 September, 1997.

Stoltzfus RJ, Dreyfuss M, Shrestha JB, Khatri SK, Schulze K, West KP Jr. Effect of maternal vitamin A or beta-carotene supplementation on iron-deficiency anemia in Nepalese pregnant women, post-partum mothers, and infants. XVIII IVACG Meeting, Cairo, Egypt 1997.

West KP Jr, Khatri SK, Katz J, LeClerq SC, Pradhan EK, Shrestha SR, Connor PB, Dali S, Adhikari R, Pokhrel RP, Sommer A. Impact of weekly supplementation of women with vitamin A or beta-carotene on fetal, infant and maternal mortality in Nepal. XVIII IVACG Meeting, Cairo, Egypt 1997.

assay was established at the Nepal Eye Hospital to quantify iodine levels, and a questionnaire was added at the 6-month post-partum visit asking about salt use and provision made to test the salt for potassium iodate content. Urinalysis was completed in FY 98.

3. *Nepal – NNIPS-3*. This cluster-randomized prevention trial will recruit, supplement and follow ~3700 pregnant women to assess the impact of daily maternal supplementation with combinations of folate, iron, zinc and multiple other micronutrients, all with vitamin A, compared to vitamin A alone on status, birthweight and infant and maternal post-partum morbidity. The trial will be able to measure a 35% or greater impact on infant mortality with certain nutrient combinations with acceptable precision.

Accomplishments: NNIPS-3 has changed during the year, since the FY 98 work plan was submitted. Originally, NNIPS-3 was to test the impact of daily multiple micronutrient supplements on fetal loss and infant mortality while continuing to enroll women in vitamin A and beta-carotene supplement groups to assess differences between supplements with respect to maternal mortality. Features of this original plan are being incorporated into a proposed trial in Bangladesh, while the “new” NNIPS-3 focuses on determining effects of antenatal supplementation with micronutrients on intrauterine growth/birth weight and other outcomes not requiring the enormous sample size of a mortality trial. The new NNIPS-3 protocol has been developed, submitted to the Committee on Human Research (JHU) for ethical approval and was approved by the Nepal Health Research Council in September 1998. The Roche/Brazil & USA and Jamieson/Canada Companies are currently preparing 1.5 million supplements. The field site, manuals and procedures were in process of being developed and tested in Nepal as of the end of the fiscal year.

4. *NNIPS-4*. In the Year 1 Work Plan, we proposed an observational cohort study investigating the association between iron status and morbidity/mortality in preschool children in south India. This was to follow the field work for the VASIN (Vitamin A Supplementation in Newborns) project in the same study area. Over the past year our thinking about the relative value of such a project has changed considerably. Under the original design, if there was an observed association of poor iron status (or mild to moderate anemia) with increased mortality or morbidity, a randomized community trial would have been needed to determine if iron supplementation in this age group would improve child survival. Given the sequential nature of these studies, it would take 8-10 years to obtain an answer to the iron and child survival question and start applying the findings to child survival programs. Concurrent with this thinking, evidence suggesting a role of zinc supplementation in reducing morbidity rates in preschool children emerged from small studies. To date, however, there are no studies that have determined if such an effect translates to a mortality reduction. Nor are there any studies investigating the potential interaction of iron and zinc, especially among a population of children already receiving routine vitamin A supplementation. The new zinc findings influenced our decision to modify this aspect of our research agenda.

Instead of the originally proposed observational study of iron status and mortality, we propose to conduct a 2x2 factorial randomized trial to investigate the effect of iron and zinc supplementation on preschool child mortality. Secondary outcomes will include morbidity, growth, and iron and zinc status. This will be conducted in a population already receiving routine vitamin A supplementation so that we can determine if there is an additional child survival benefit that can be achieved by also dosing preschool children with iron and/or zinc.

The venue for the trial has also been changed from south India to southern Nepal, an existing primary research site under this cooperative agreement. This was done to improve the cost-efficiency of the study since child mortality rates are significantly higher in Nepal than southern India, resulting in a smaller sample size requirement. In addition, the move to the Sarlahi study area in Nepal will result in significant start-up savings since the field research infrastructure is already in

place and the field teams already have experience in conducting studies of preschool child mortality (i.e. NNIPS-1).

Accomplishments: This trial is currently in the early planning phase and is scheduled to follow the field work of NNIPS-3. We expect to begin field operations for this project in late 1999 with the total data collection phase to take approximately 2 ½ years. Protocols will be submitted by the end of 1998 to the ethical review committees at Johns Hopkins University and to the Nepal National Health Research Council.

5. **DIVA.** Goals of identifying dietary and other behavioral determinants of risk are being pursued most clearly in the Nepal –DIVA data which consists of 7-8 days of direct observation and 4 7-day food frequencies to assess child and family intakes in their home settings (n=~100 case and control families). Half-dozen papers have been published from the DIVA study in the past year. Dietary intake is being related to household, maternal and child behavioral risk factors that, in turn, may provide some new ideas and evidence for reshaping nutrition education approaches in the future.

Accomplishments: Data analysis was performed to help to identify dietary and other high risk behavioral patterns underlying VA deficiency. Manuscripts were produced and published².

6. **Etiologic studies of anemia in pregnancy, lactation and infancy:** This study will determine the extent and relative importance of intestinal and malarial parasitism, diet and other aspects of nutritional status in placing women and their infants at risk of iron deficiency and anemia. Findings from the study will help in developing approaches to assessing causes of maternal anemia and appropriate control interventions in South Asian countries.

Accomplishments: Field work, carried out as part of NNIPS-2, is complete. Definitive data analysis was initiated. Manuscripts were prepared for publication.

7. **Biologic basis for impact of VA on anemia:** This study will investigate the mechanisms through which VA deficiency is likely to cause anemia and disturbances of iron metabolism. At present,

² Gittelsohn, J., Mookherji, S. and Pelto, G. "From Macro to Micro Assessment of Food Security: Operationalizing Household Food Security in Rural Nepal." (Submitted to Food and Nutrition Bulletin, July 1997; resubmitted June 1998).

Shankar, A.V., Gittelsohn, J., Pradhan, R., Dahal, B., West, K.P. Jr. "Night Blindness, Diet and Health in Nepalese Children: An Ethno-epidemiological Investigation of local Beliefs," Ecology of Food and Nutrition (in press).

Gittelsohn, J., Shankar, A.V., West, Jr., K.P., Faroukh, F., Gnawali, T., and Pradhan, E. "Child Feeding and Care Behaviors are Associated with Xerophthalmia in Rural Nepal." Social Science and Medicine. (in press).

Shankar, A.V., Gittelsohn, J., West, K.P. Jr., Stallings, R., Gnywali, T and Faruque, F. "Eating from a shared plate impacts food consumption in vitamin A deficient Nepali children." The Journal of Nutrition. (in press).

Shankar, A.V., Gittelsohn, J., Pradhan, E.K., Dhungel, C. and West, K.P. Jr. (1998) "Home Gardening and Animal Access Among Xerophthalmic Households in Rural Nepal." Food and Nutrition Bulletin, 19(1): 34-41.

Gittelsohn, J., Shankar, A.V., West Jr., K.P., Ram, R., Dhungel, C. and Dahal, B. (1997) "Infant Feeding History Reflects Antecedent Risk of Xerophthalmia in Nepali Children," European Journal of Clinical Nutrition, 51: 484-490.

Gittelsohn, J., Shankar, A.V., Ram, R., Gnywali, T. and West, K.P. (1997) "Estimating Reactivity and its Effects in Direct Observation Studies of Health Behavior," Human Organization, v.56(2): 182-189.

Gittelsohn, J., Thapa, M. and Landman, L.T. (1997) "Cultural Factors, Caloric Intake and Micronutrient Sufficiency in Rural Nepali Households." Social Science and Medicine, v.44(11): 1739-1749.

these mechanisms are not well-understood. Most recently, the NNIPS-2 study has documented a large reduction in anemia in vitamin A-supplemented pregnant women who were not infected with hookworms. This study will use archived serum samples from these women to test the hypotheses that vitamin A acts on anemia through modulation of the inflammatory response and/or the secretion of erythropoietin in response to anemia. Findings may help improve understanding of the role of VA supplementation in anemia control programs.

Accomplishments: Manuscript was drafted for publication.

8. **Nepal-Maternal zinc treatment trial for night blindness:** This study is assessing the efficacy of a 3-week regimen of daily maternal zinc supplementation for curing XN during pregnancy. Findings will shed light on the degree to which maternal XN in rural South Asia is due to underlying zinc deficiency. Field work co-funded by the Nestle Foundation.

Accomplishments: Field work and biochemical analyses were completed. Data analysis was started.

Bangladesh

1. ***Maternal vitamin A, beta-carotene and multi-nutrient supplementation trial:*** This large field trial will serve to confirm the findings of NNIPS-2 on maternal mortality and advance knowledge about the impact of multi-nutrient supplementation of pregnant and lactating women on fetal and infant growth, morbidity and mortality, and maternal morbidity, status and mortality in a second malnourished population of women in South Asia.

Accomplishments: A trip was made to Bangladesh to explore the possibility of conducting the field trial there, with positive early responses from the USAID Mission and potential collaborators in-country. Correspondence continued through September 1998 that provided an subsequent opportunity to visit the country in November 1998, as a scheduled visit in September was cancelled due to severe flooding at that time. In the next visit, we will focus on government and continued USAID/Dhaka interest in the proposed study, potential study sites, alternative designs for the trial(s) that can permit answers to be obtained efficiently, mechanisms of collaboration, etc. A formal protocol will be drafted in the first half of FY 99.

2. ***Impact of maternal post-partum vitamin A and beta-carotene supplementation on maternal and infant status:*** This randomized trial assessed the effects of a single high-dose of VA given to mothers immediately post-partum and daily, dietary level, beta-carotene supplements given to mothers up to 9 months post-partum on biochemical indicators of maternal and infant VA status. Findings could help to refine policies regarding VA supplementation and dietary carotenoid intakes for post-partum women.

Accomplishments: The field work, laboratory and primary study analysis for this study was completed. A manuscript³ reporting the main effects of supplementation was submitted (and subsequently accepted by the Journal of Nutrition) for publication.

India

1. **Vitamin A Supplementation in Newborns Study (VASIN), Tamil Nadu, India:** This study aims to evaluate the impact of administering a 50,000 IU dose of VA to newborns on early infant mortality. It follows from two previous studies—NNIPS-1 and the Indonesia Newborn Vitamin A supplementation trial—that yielded mixed findings. If this project demonstrates that supplementation

³ Rice AL, Stoltzfus RJ, de Francisco A, Chakraborty J, Kjolhede CL, Wahed MA. (1998) Maternal vitamin A or β -carotene supplementation in lactating Bangladeshi women benefits mothers and infants, but does not prevent subclinical deficiency

of newborns with vitamin will reduce early infant mortality, then policy recommendations regarding inclusion of supplements in birthing kits and other approaches to encouraging such early supplementation would be appropriate.

Accomplishments: The recruitment and data collection phase of the project got underway. As of mid-October, 1998, approximately 1750 pregnant women were identified and agreed to participate in the project. Between 100 and 130 newly pregnant women are being identified each week. The total number of live births enrolled is approximately 550 with between 80 and 90 live births occurring in the study area each week. Total target study population is 6000 live births.

Philippines

1. **Vitamin A-fortified Pandesal Trial:** This randomized, double-masked clinical trial evaluated the efficacy of vitamin A-fortified wheat-flour bread (called pandesal, the locally baked "national bread" in the Philippines) in improving vitamin A (VA) status. Study collaborators included the Nutrition Center of the Philippines and Helen Keller International. The JHU costs for this OMNI Field Support research project were partially supported by the MHCA.

Accomplishments: The study was initiated in September 1997 and fieldwork was completed in April 1998. JHU provided technical assistance (beyond managing the HKI/Nutrition Center for the Philippines OMNI subcontract). Serum retinol analysis was carried out in May 98 (by Neal Craft), and initial data analysis and initial reporting was completed in September 98. The study enrolled and randomized approximately 900 school-aged Filipino children to receive a 60 gram piece of pandesal, either VA-fortified (intervention) or non-fortified (control), 5 days per week for 6 months. The VA-fortified pandesal contained ~133 (g of retinol equivalents (RE) per serving (~33% of the RDA). Children in both groups consumed, on average, nearly all of the pandesal offered to them. Serum retinol levels showed a slight shift toward more adequate levels as a result of VA-fortified pandesal intake. Improved VA status, however, was most evident by findings using the modified relative dose response (MRDR) which provides an indirect estimate of the adequacy of liver vitamin A stores. This test showed that VA-fortified pandesal intake halved the percent of children with inadequate liver vitamin A stores (15.3% vs. 28.6%, $p=0.05$). The results showed that the vitamin A status of children can be improved when they consume vitamin A-fortified pandesal. The trial provides scientific evidence to support the fortification of wheat flour with vitamin A in the Philippines as an effective means to improve vitamin A status of the population. This trial aimed to determine the efficacy of vitamin A-fortified wheat-flour breads ("pandesal") in improving vitamin A status in school-age children

Thailand

1. **Dietary Studies in Women:** These studies aimed to evaluate the impact of carotenoid rich diets in improving total body stores of vitamin A in lactating women ($n\approx 90$) as a means to evaluate nutritional effects of dietary guidelines that promote similar types of dietary intakes.
Accomplishments: Fieldwork was completed in February 1998 for this randomized clinical trial. Total body retinol stores currently being assessed by using stable isotopic labels (deuterated retinol), in collaboration with INMU at Mahidol University (partly funded by the IAEA).

2.2 Africa

Zimbabwe

1. **ZVITAMBO Project (Main trial):** This large trial of over 12,000 mother-newborn pairs, comprising both HIV+ and HIV- mothers, is assessing the impact of administering a single oral dose of VA to mothers or neonates immediately after birth, in a 2x2 factorial design, on infant mortality, mother-to-child HIV transmission during breast feeding, and maternal HIV infection during the first 2 years partum year (co-funded by USAID, CIDA and the NIH), and sexually transmitted HIV infection among post partum women. In a sub-study among 400 HIV-infected lactating women, the study will assess the impact of vitamin A supplementation on viral load in plasma and breastmilk, and on CD4/CD8 counts, while controlling for serum retinol and markers of the acute phase of infection.

Accomplishments: The trial is in progress. Major accomplishments in year 1 include:

- **Recruitment of study subjects.** Recruitment began November 1997. As of October 1, 1998, nearly 6000 mother-infant pairs had been enrolled.
- **Renovated, furnished, and equipped a clinic of the Harare City Health Department for carrying out ZVITAMBO follow up visits.** 25 nurse midwives staff the clinic. A home visit system of 7 teams (nurse+aide+driver+car) are coordinated from this clinic to follow up defaulters. About 25% of all follow up visits are conducted in homes. The clinic will return to City Health in its fully refurbished state at the end of the project.
- **Established a state-of-the-art data management shop that computerizes all the information collected in the study.** A total of 1.8 million pages of data collection forms will be processed during the study (over 3000 pages per day during the peak of the study). The system uses Image Data Entry with automated programs for data cleaning and storage.
- **The Data Safety and Monitoring Committee (Chair: Prof. G. Beaton) completed 4 interim review of major outcomes.** They conclude, thus far, "...No evidence of harmful effect of vitamin A administration was found, and suggests that the project carry on with the present design."

There were some major issues/modifications in project plan resulting from a UNAIDS meeting in April 1998 to develop guidelines for infant feeding in the context of maternal HIV infection. The new guidelines represent a substantial shift in UN policy toward supporting alternatives to breast feeding for infants of HIV+ mothers. We carefully examined implications for ZVITAMBO and made some changes in our protocol. We now offer women newly recruited to ZVITAMBO the opportunity to know their HIV status by the following business day, to facilitate their making an informed decision before commencing breast feeding. Draft teaching/counseling materials were drafted and are in use. Workshops for project nurses to provide them with technical knowledge and skills to counsel women around this issue were held. A proposal has been submitted to Linkages and DFID to carry out a qualitative research study by a social scientist and a counseling expert. The project will identify constraints to Zimbabwean women NOT breast feeding, consult decision makers in the family unit (mothers-in-law, husbands), develop and test a counseling method of creating "fully informed women", and train Zimbabwean health professionals in these skills.

2. **Zvitambo project (Immunologic component):** In support of the main Zvitambo project, an immunologic component of the study is being undertaken. Under this component, supportive immunologic assays are being performed on blood and breastmilk samples at the Harare Hospital (ELISAs, flow cytometry for CD4/CD8, and Western blot) and PCR assays to diagnose HIV infection and viral load in plasma and breastmilk will be carried out in the Department of Pediatrics, University of Zimbabwe throughout the study period. (Co-funded by USAID, CIDA and NIH).

Accomplishments: Clinical trial is in progress. The project established 3 laboratories within Zimbabwean institutions in which Zimbabwean scientists will carry out all assays for ZVITAMBO. At the close of the project, functioning laboratories will remain in Harare Central Hospital (HIV diagnostic laboratory), the University of Zimbabwe School of Medicine (Polymerase Chain reaction laboratory), and the Department of Nutrition, University of Zimbabwe (VA laboratory).

- Harare Central Hospital is the largest public sector referral hospital in the country. It is being equipped and enabled to carry out ELISAs, HIV rapid tests, CD4/CD8 FACs count, and Western blot with state of the art equipment. It will also be capable to receive, process, and archive samples using a completely bar-code controlled computerized system.
- The University of Zimbabwe School of Medicine is serving as the polymerase chain reaction laboratory. HIV RNA (viral load), the gold standard method of monitoring progression to AIDs, will be measured in plasma and breastmilk in this laboratory. HIV DNA is the only definitive method of diagnosing infants, but it has had limited application in Africa because the kits worked well in detecting only the strains of HIV prevalent in North America and Europe. During this reporting period, we validated a new kit designed to detect a large spectrum of HIV strains and documented extremely high sensitivity and specificity in detecting the strain common in Southern Africa. For the first time, Zimbabwe has the capability to diagnose HIV in its infants. The laboratory is being certified by Roche and will participate in the ACTG external QC program at Rush Presbyterian Hospital, Chicago.
- The project installed all equipment and supplies needed to assay retinol in serum and breastmilk and analyze A2 for the MRDR test at the Department of Nutrition, University of Zimbabwe. This lab has also begun measuring markers of the acute phase of infection. The lab participates in the National Institutes of Standards and Technology (NIST) EQC program.

Malawi

1. **Maternal VA supplementation trial on HIV and birth outcomes (Main trial):** This randomized trial assessed the impact of low-dose maternal VA supplementation during pregnancy on mother-to-child HIV transmission, perinatal mortality and birthweight. Findings will provide a basis for whether maternal VA supplementation during pregnancy can lower vertical HIV transmission and improve maternal and infant health outcomes during HIV infection (field work fully funded under a NIH grant).

Accomplishments: Data and laboratory analyses were performed.

2. **Maternal VA supplementation trial on HIV and birth outcomes (Immunologic component):** The effects of antenatal VA supplementation on immune factors in breastmilk (e.g., lack of lysozymes, lactoferrin, secretory leukocyte protease inhibitor) will be investigated from ~600 of 900 participants of the recently completed trial in Malawi (Primarily supported by NIH).

Accomplishments: Biological specimens were collected and partially analyzed.

3. **Micronutrients for TB and HIV, Malawi:** The purpose of this study is to determine if adjunct micronutrient supplementation along with triple TB chemotherapy can further reduce morbidity and mortality from HIV-associated pulmonary tuberculosis in adults (field and laboratory work supported by NIH)

Accomplishments: Planning and training in progress.

Uganda

1. **Early childhood VA supplementation trial:** This field trial will determine the efficacy of VA as targeted therapy for reducing the progression of disease (as opposed to upregulating HIV, as some small studies have suggested) and survival in HIV-infected preschool (6-36 month old) children. Findings may help provide impetus for VA supplementation of HIV-infected infants (field work fully funded under a NIH grant).
Accomplishments: Study is in progress.

Tanzania

1. **Tanzania (Zanzibar) - Schoolers Study:** This study assessed the impact of a school-based de-worming program on growth in school children and provides strong evidence for hookworm control as a strategy to control iron deficiency anemia in African school children.
Accomplishments: Surveillance of the study cohort was undertaken.
2. **Tanzania (Zanzibar) - TAPP (Trial of anemia prevention in preschoolers):** This study will assess the impact of iron supplementation and/or de-worming in preschool children on iron status and growth. It will address the efficacy of community-based interventions in a preschool population for whom interventions to control anemia are not routinely implemented.
Accomplishments: Data analysis was conducted. Serum retinol samples were analyzed.
3. **One Plus:** This study will assess the impact of weekly and daily school-based iron supplementation on children's school attendance, cognition and learning. The study will also assess the additional impact of iron supplementation in a setting with an established school-based de-worming program. Compared to previous studies, this trial will make several unique contributions: it will document the impact of iron deficiency on learning in a population where iron deficiency anemia is severe and it will compare the impact of weekly vs. daily supplementation on cognition and learning, which has never been done. Field costs for this trial will be funded by the Micronutrient Initiative. The MHCA is providing core support to JHU for development of cognitive assessment tools appropriate for children in rural Africa.
Accomplishments: Field activities are underway.
4. **Prenatal iron and anthelmintic trial:** This study will determine the impact of prenatal iron supplementation alone or in conjunction with anthelmintic therapy on pregnancy outcomes (low birthweight, severe anemia of pregnancy). If beneficial, helminth control could be added to prenatal iron supplementation programs. The trial will be carried out in Pemba Island, where iron deficiency and hookworm infection are known to be endemic.
Accomplishments: Early planning stages for this trial were undertaken.

Ghana

1. **Ghana - Malaria:** The aim of this study is to evaluate the impact of zinc and VA supplementation on malaria morbidity under hyper-endemic conditions of malaria transmission in Africa. In addition, the study proposes to investigate if zinc supplementation given with iron will mitigate any exacerbative effects of iron on malaria and optimally promote zinc, iron and vitamin A status and growth in young infants. Immunologic studies will be integrated into these trials to allow an understanding of the mechanism underlying the effects of VA and zinc. This information will be

used to facilitate design of nutrient-based interventions for malaria and for vaccine development. Additional studies are being planned regarding the effects of maternal zinc supplementation on maternal malaria and on the health of infants born of zinc-supplemented mothers.

Accomplishments: The possibility of a vitamin A-zinc intervention trial on malaria was explored in Ghana. Working relationships have been established with the Kintampo Health Research Center and the Noguchi Memorial Institute of Medical Research. Preliminary data have been collected and a study protocol was developed. Proposals for the child trial are currently under review at various agencies and joint NIH, Thrasher, and USAID funding is anticipated. Proposals for the maternal trial are in preparation.

2.3 Latin America

El Salvador

1. **Influenza vaccine and VA supplementation trial:** This randomized trial will assess the effect of VA supplementation on the response to two different formulations of Hi-B vaccines in infants. Findings from this study will help determine if VA supplementation of infants can enhance a child's H. influenza vaccine response. In addition the studies will facilitate identification of vaccine formulations which synergize with VA. Additional surveys are planned to more clearly document the public health importance of the 10-15% maternal night blindness already documented as part of the vaccine trial.

Accomplishments: Enrollment of study children was started.

Peru

1. **Maternal zinc trial + iron:** This study was a demonstration program of prenatal iron supplementation with the new INACG guidelines. Findings demonstrated programmatic benefits of new INACG guidelines generalizable to the LAC region and elsewhere.

Accomplishments: A manuscript was prepared for publication⁴.

2. **Iron status of infants of iron-supplemented mothers:** This study assessed the potential benefits to iron status of infants of mothers who were supplemented with daily iron (60 mg) during pregnancy.

Accomplishments: Data analysis is on-going. Manuscripts being prepared for publication.

3. **Maternal zinc supplementation trial-1:** This study investigated the effects of supplementing mothers prenatally through the first four weeks post-partum with 15 mg zinc (added to 60 mg iron and 250 µg folate) on birth outcomes, infant morbidity, growth and development. The findings have helped define the benefits of giving zinc in prenatal supplements for maternal and infant health.

Accomplishments: Intensive data analysis was performed and manuscripts were drafted and are in press, submitted or in preparation.⁵

⁴ Zavaleta N, Caulfield LE, Garcia T. Hematologic changes during pregnancy in Peruvian women receiving prenatal iron and folate supplements with or without zinc. *Am J Clin Nutr* (submitted).

⁵ Caulfield LE, Zavaleta N, Shankar A, Meriardi M. The potential contribution of maternal zinc supplementation during pregnancy for maternal and child survival. *Am J Clin Nutr* 1998;68: 499-508.

4. **Maternal zinc supplementation trial-2** This study will assess the effects of supplementing mothers prenatally through the first 4 weeks post-partum with 25 mg zinc (added to 60 mg iron and 250 µg folate) on fetal development, and infant morbidity, growth and development.

Accomplishments: Data collection was started. Funds from Nestle Foundation and USDA were sourced to initiate trial.

2.4 Oceania

Papua New Guinea

1. **Impact of preschool zinc supplementation on malaria incidence and severity:** This randomized trial assessed the impact of Zinc supplementation on malaria attack rates, severity and immunologic indices of malaria infection, and other child health outcomes. Findings will strengthen justification for supplementing children with zinc in malaria-endemic regions and could assist in developing a more effective malaria vaccine.

Accomplishments: Field work completed. First manuscript on impact of Zinc on malaria incidence (clinic attack rates) and severity of illness currently soon to be submitted for publication (Shankar, A.H., B. Genton, L. Wu, K.P. West, J. Tielsch, and M.P. Alpers. The influence of zinc supplementation on malaria morbidity in preschool children in Papua New Guinea.

3. New Assessment Techniques

- 3.1 **Maternal Night Blindness (XN) studies:** Studies carried out in Nepal have reported on the extent, consequences, risk factors and ethnography of maternal night blindness (XN), which have stimulated global interest in maternal XN as a diagnostic and prognostic indicator of maternal health and nutritional risk.

Accomplishments: Fieldwork and analyses for these studies were completed, manuscripts⁶ were produced and published.

Menaldi M, Caulfield LE, Zavaleta N, Figueroa A, DiPietro J. Adding zinc to prenatal iron and folate supplements improves fetal neurobehavioral development. *Am J Obstet Gynecol* 1998; (in press).

O'Brien KO, Zavaleta N, Caulfield LE, Yang DX, Abrams SA. The influence of prenatal iron and zinc supplement on absorption of supplemental iron, red blood cell incorporation and iron status in pregnant Peruvian women. *Am J Clin Nutr* 1998; (in press).

Caulfield LE, Zavaleta N, Rivera K. Adding zinc to prenatal iron and folate supplements improves maternal and neonatal zinc status in a Peruvian population. *Am J Clin Nutr* (in press).

Caulfield LE, Zavaleta N, Figueroa A, Leon Z. Adding zinc to prenatal iron and folate supplements does not affect duration of pregnancy or size at birth in Peru. *J Nutr* (submitted).

- 6 Christian P, Bentley ME, Pradhan R, West KP, Jr. An ethnographic study of night blindness 'ratauni' among women in the terai of Nepal. *Soc Sci Med* 1998; 7:879-889.

Christian P, West KP, Jr., Khatri SK, Katz J, Shrestha SR, Pradhan EK, LeClerq SC, Pokhrel RP. Night blindness of pregnancy in rural Nepal - nutritional and health risks. *Int J Epi* 1998; 27:231-237.

Christian P, Schulze KJ, Stoltzfus RJ, West KP Jr. Hyporetinemia, illness symptoms, and acute phase protein response in pregnant women with and without night blindness. *Am J Clin Nutr* 1998; 67:1237-1243.

Christian P, Thorne-Lyman AL, West KP Jr., Bentley ME, Khatri SK, Pradhan EK, LeClerq SC, Shrestha SR. Working after the sun goes down: Exploring how night blindness impairs women's work activities in rural Nepal. *Eur J Clin Nutr* 1998 52:1-6.

West KP Jr, Christian P. Maternal night blindness: extent and associated risk factors. IVACG Statement, International Vitamin A Consultative Group. Washington DC, 1998.

- 3.2 **Blood spot:** JHU has been collecting blood spots on filter paper in studies in Nepal over the past 4 years, most of which have an accompanying serum sample for retinol determination.
Accomplishments: Retinol values in blood spots have been correlated with serum retinol levels by HPLC. The work is being done in collaboration with Dr. Neal Craft in North Carolina. Preliminary findings were reported during the IVACG meeting in Cairo⁷ and the Experimental Biology Meeting '98, and a draft manuscript was started.
- 3.3 **Dark Adaptometry:** Non-invasive assessment of VA status in individuals and communities is a priority issue amidst the HIV pandemic. A portable dark adaptometer to non-invasively determine early scopic vision loss resulting from VA deficiency has been developed and initially tested in Indonesia and India (reports published in the Am J Clin Nutr in 1995 and 1997). Additional studies were planned and, to-date, have been carried out in Nepal and Thailand.
Accomplishments: In Nepal, dark adaoptometry assessment was built into the sub-sample studies of NNIPS-2. Data underwent preliminary analysis with preliminary findings showing additional promise for the method in assessing high risk women and being responsive to supplementation. Dark adaptometry was used in a second randomized trial in Nepal (Sarlahi) that evaluated the effects of maternal zinc supplementation in curing night blindness. Data were prepared for analysis. In Thailand (in collaboration with Mahidol University), dark adaptometry, serum retinol and MRDR was measured in young children.
- 3.4 **Breastmilk vitamin A concentration:** Previous work suggests that breastmilk VA concentration has the potential to be a useful indicator of VA status. Several studies (in Nepal, Bangladesh and Zimbabwe) will provide further data with which to evaluate the performance of breastmilk retinol as an indicator of both maternal and infant VA status.
Accomplishments: Breastmilk specimens from a post-partum maternal supplementation trial in Bangladesh were biochemically analyzed and preliminaray data analysis was conducted. From NNIPS-2, breastmilk specimens were analyzed for retinol and carotenoid concentration. In Zimbabwe, breastmilk specimens were collected as part of the ZVITAMBO study.
- 3.5 **Stable isotopes:** JHU will continue working with the Institute of Nutrition at Mahidol University on an ongoing field trial that is evaluating the efficacy of different vitamin A-containing diets to change total body stores of vitamin A as measured indirectly by stable isotope dilution (supported in part by IAEA).
Accomplishments: Fieldwork was completed. Stable isotope analysis is being conducted at the University of California – Davis.
- 3.6 **Conjunctival impression cytology (CIC):** Originally developed at JHU as a non-invasive tool for vitamin A status assessment, it appears to be a valid technique for estimating the prevalence of sub-clinical VA deficiency, but its responsiveness to intervention has been variable in different settings.

Christian P. West KP Jr, Khattry SK, Katz J, LeClerq S, Pradhan EK, Shrestha SR. The impact of low dose maternal vitamin A or beta-carotene on night blindness during pregnancy and the post-partum period in Nepal. J Nutr 1998 (in press).

Khattry SK, Shrestha SR, LeClerq S, Pradhan EK, Chrisuan P, West KP. Maternal night blindness in Nepal. J Nepal Med Assoc 1998 (in press).

⁷ Craft, NE., S. Yamini, JH. Humphrey, ML. Dreyfuss, KP. West, Jr. 1997. Analysis of vitamin A in dried blood spots by HPLC. XVIII IVACG Meeting.

Accomplishments: CIC was done in the clinic sub-sample of women in NNIPS-2 (1000 samples). These still need to be stained, mounted and read. Once done, these data will be used to further examine the prevalence and response to VA and beta-carotene interventions.

3.7 Dietary Assessment: JHU has incorporated dietary assessment into most large population-based studies and field trials. Techniques most commonly adopted are 7-day or usual food frequencies and 24 hour recalls. Direct observation data exist, in addition to 7-day food frequencies, for one large ethnographic study of dietary patterns and VA deficiency in Nepal (DIVA). These data provide a basis for assessing reliability and measures of "validity", the latter using biochemical or clinical status to define referent groups.

Accomplishments: Dietary data bases exist on studies conducted in Indonesia, Philippines, Nepal, Thailand, Zambia, Tanzania, Malawi, Uganda, Peru and PNG. Each data set is in a different phase of use but most remain active data bases. Recent dietary data from NNIPS-2 and DIVA studies in Nepal are undergoing active and extensive analysis. DIVA dietary data can be found in several publications over the past 18 months, including papers on technique validity. Reproducibility analysis is continuing. Recent merger of food composition data, based on local foods that were analyzed at Craft Industries in the USA plus other reputable sources, provide new opportunities to estimate nutrient intakes by both food frequency and direct observational methods covering a 1-year period of assessment. Also, preliminary analysis of 7-day food frequency and 24-hour recall data from NNIPS-2 show close correspondence with circulating retinol and carotenoid concentrations, providing a degree of validity.

Previous DIVA/Nepal data were prepared and analyzed to validate repeated 7-day food frequency intakes of children against intakes estimated by direct observation throughout a 12-month period of observation.

4. Core Activities

4.1 Laboratory

The laboratory supporting biochemical analyses of the MHCA-supported field trials continued to process a large volume of samples during this fiscal year as evidenced by the list below. Under the direction of Dr. Essie Yamini, Li-Ming Zhou, M.S. maintained the HPLC equipment and processed samples.

- 1. Nepal/NNIPS-2:** During FY98, all serum retinol/vitamin E and carotenoids for pregnant (~1300), post partum (~1200) and infant (~700) were completed, as well as serum ferritin for the all. Serum retinoic acid levels were analyzed for ~300 pregnant and 250 post partum women; breastmilk retinol and carotenoids on ~200 samples were carried out for the maternal night blindness sub-studies, and ~200 blood spot retinol/carotenoids were completed.
- 2. Nepal/ XN-zinc trial:** During the first year of the MHCA, laboratory activities supported the zinc supplementation trial and analyzed ~400 samples from each study arm for serum zinc, urinary zinc, urinary creatinine, serum ferritin, serum RBP, serum retinol/vitaminE and carotenoids. Resources from the Nestle Foundation helped support these analyses. (N=~400 for each).
- 3. PNG Zinc trial:** About 800 samples were analyzed for serum retinol/vitamin E/carotenoids and serum zinc.

4.2. Data Management and Analysis

During the first year of the MHCA the data processing unit accomplished the following three major tasks (in addition to the routine data management and analysis support provided to all MHCA-related research projects):

1. Purchased and initial set-up a new Sun Server to replace the Solbourne system. The purchase was delayed by about 6 months from initial plans resulting in savings of over 20% and the acquisition of an additional CPU for no additional cost.
2. Completed a major review of our data processing software needs for both field locations and at the central facility (JHU). The data management team decided to continue using Paradox for DOS at the Nepal facility for the duration of the NNIPS-3 project due to limited trial start-up time. Access and Visual Basic will replace paradox for DOS for the NNIPS-4 study, which will likely be operative in the field by late 1999. Use of Paradox for DOS will also be continued at our field site on Pemba Island, Zanzibar given the limited physical and personnel infrastructure there. This situation will be reassessed as further projects come on-line in Pemba. The anticipated maternal mortality trial in Bangladesh will be supported using the new Access-Visual Basic combination.
3. Obtained additional formal training for our key data processing staff. Andre Hackman and Gwendolyn Clemens attended basic epidemiology and biostatistics courses at the Johns Hopkins Summer Institute of Epidemiology in 1998 and Lisa Pradhan, the Nepal field station data center manager, also took additional epidemiology courses at Johns Hopkins during the summer term. She has now almost completed her requirements for the MPH.

4.3 Publications

During the 1997 and 1998 (through September) JHU published 75 manuscripts (28 in CY97 and 47 in CY98) that reported findings from its applied vitamin A, iron and anemia, zinc, iodine, other dietary and nutritional research program. Appendix 2 lists those published in CY97 and Appendix 3 contains those published or in press during the period of January to September 1998. As in the past, we expect these publications provided a base of evidence on which policies were reshaped and new alternatives pursued.

4.4 Technical Assistance

On a regular basis, JHU nutrition faculty provide technical assistance and policy guidance to agencies such as UNICEF, WHO, IDRC, HKI, IEF, ICDDR, OMNI, IFPRI and others. During this reporting period, assistance was provided to UNICEF-Philippines (maternal night blindness questionnaire), Save the Children USA, Mahidol University (dark adaptometry), DHS (questions on nutrition), CORE Group (micronutrient presentations), HKI/Bangladesh (fortification of food aid), Indonesia MOH (community eye care program), Morocco MOH representative (analysis of VA data) as well as others (see Appendix 7).

4.5 Teaching

Drs. West, Gittelsohn, Stoltzfus, Caulfield, Christian, Shankar and Tielsch are teaching courses in the School of Hygiene and Public Health which include extensive material on vitamin A and other micronutrient deficiencies.

4.6 Advocacy

At the very end of FY97 Dean Alfred Sommer was awarded the highly prestigious Albert Lasker Clinical Medical Research Award, the Helmut Horten Medical Research Award, and the Prince Mahidol Award for International Contributions to Medicine and Public Health. These served to highlight the advancements in vitamin A research to promote child survival in the developing world under USAID support.

Two JHU/USAID field studies were featured prominently in the 1998 UNICEF State of the World's Children Report: the NNIPS-2 trial that showed a 40% reduction in maternal mortality with vitamin A/beta-carotene supplementation in Nepal, and the zinc supplementation trial in Papua New Guinea that found a 40% reduction in clinical malaria attack rates in young children. The NNIPS-2 trial also "headlined" the UNICEF State of the World's Children video for 1998. These types of exposures of research and their findings to the global lay public have served to maintain high visibility for the roles of micronutrients in health and nutrition in women's health over the past year.

Appendices

APPENDIX 1

FINANCIAL SUMMARY

APPENDIX 2

LIST OF 1997 PUBLICATIONS

1997 Publications

Peer-reviewed journals

Vitamin A

1. Gittelsohn J, Shankar AV, West KP Jr., Ram R, Dhungel C, Dahal, B. Infant feeding history reflects antecedent risk of xerophthalmia in Nepali children. *Eur J Clin Nutr* 1997;51:484-490.
2. Greenberg BL, Semba RD, Schoenbaum E, Klein RS. Vitamin A deficiency among former and current injecting drug users in Bronx, New York. *Nutr Res* 1997;17:785-796.
3. Katz J, Yoon SS, Brendel K, West KP, Jr. Sampling designs for xerophthalmia prevalence surveys. *Int J Epidemiol* 1997;26:1041-1048.
4. Sanchez AM, Congdon NG, Sommer A, et al. Pupillary threshold as an index of population vitamin A status among children in India. *Am J Clin Nutr* 1997;65:61-66.
5. Semba RD, Akib A, Beeler J, Munasir Z, Permaesih D, Muherdiyantiningsih, Komala, Martuti S, Muhilal. Effect of vitamin A supplementation and measles vaccination in nine-month-old infants. *Public Health* 1997;111:245-247.
6. Sommer A. Vitamin A prophylaxis. *Arch of Disease in Childhood* 1997;77:191-194.
7. Sommer A, West KP Jr. The duration of the effect of vitamin A supplementation [letter; comment]. *Am J Pub Hlth* 1997;87:467-469.
8. Sommer A. Vitamin A deficiency, child health, and survival. *Nutrition* 1997;13:484-485.
9. West KP Jr., LeClerq SC, Shrestha SR, Wu LS, Pradhan EK, Khatry SK, Katz J, Adhikari R, Sommer A. Effects of vitamin A on growth of vitamin A deficient children: field studies in Nepal. *J Nutr* 1997;10:1957-1965.

Vitamin A and HIV

10. Semba RD, Miotti PG, Chipangwi JD, Liomba G, Yang LP, Wu CO, Hoover DR. Maternal vitamin A deficiency and child growth failure during human immunodeficiency virus infection. *J of Acquired Immune Deficiency Syndromes and Human Retrovirology* 1997;14:219-222.
11. Semba RD. Vitamin A and human immunodeficiency virus infection. *Proceedings of the Nutrition Society* 1997;56:459-469.
12. Semba RD. An overview of the potential role of vitamin A in mother-to-child transmission of HIV-1. *Acta Paediatrica (Suppl)* 1997;421:107-112.
13. Tang AM, Graham NMH, Semba RD, Saah AJ. Association between serum vitamin A and E levels and HIV-1 disease progression. *AIDS* 1997;11:613-620.

Iron Deficiency and Anemia

14. Stoltzfus RJ, Chwaya HM, Albonico M, Schulze K, Savioli L, Tielsch J. Serum ferritin, erythrocyte protoporphyrin and hemoglobin are valid indicators of iron status of school children in a malaria-holoendemic population. *J Nutr* 1997;127:293-298.
15. Stoltzfus RJ. Rethinking anaemia surveillance. *Lancet* 1997; 349:1764-1766.
16. Stoltzfus RJ, Dreyfuss ML, Jorgensen T, Chwaya HM, Albonico M. Hookworm control as a strategy to prevent iron deficiency. *Nutr Rev* 1997;55:223-232.
17. Stoltzfus RJ, Chwaya HM, Tielsch JM, Schulze KJ, Albonico M, Savioli L. Epidemiology of iron deficiency anemia in Zanzibari school children: the importance of hookworms. *Am J Clin Nutr* 1997;65:153-159.

Iodine Deficiency

18. Cobra C, Muhilal, Kusnandi, Rustama D, Djatnika, Suwardi SS, Permaesih D, Muherdiyantiningsih, Martuti S, Semba RD. Infant survival is improved by oral iodine supplementation. *J Nutr* 1997;127:574-578.

Other

19. Albonico M, Chwaya HN, Montresor A, Stoltzfus RJ, Tielsch J, Alawi KS, Savioli L. Parasitic infections in Pemba Island schoolchildren. *E African Med J* 1997;74:294-298.
20. Gittelsohn J, Shankar AV, West KP Jr, Ram RM, Gnywali T. Estimating reactivity and its effects in direct observation studies of health behaviors. *Human Organization* 1997;56:182-189.
21. Gittelsohn, J., Thapa, M. and Landman, L.T. Cultural factors, caloric intake and micronutrient sufficiency in rural Nepali households. *Soc Sci Med* 1997;44:1739-1749.
22. Habicht J-P, Stoltzfus RJ. What do indicators indicate? *Am J Clin Nutr* 1997;66:190-191.
23. Stoltzfus RJ, Albonico M, Tielsch JM, Chwaya JM, Savioli L. Linear growth retardation in Zanzibari school children. *J Nutr* 1997;127:1099-1105.
24. Stoltzfus RJ, Albonico M, Tielsch JT, Chwaya HM, Savioli L. School-based deworming program yields small improvement in growth of Zanzibari school children after one year. *J Nutr* 1997;127:2187-2193.
25. Tay-Kearney ML, Enger C, Semba RD, Royal W, Dunn JP, Jabs DA. T-cell subsets and CMV retinitis in HIV-infected patients. *J Infect Dis* 1997;176:790-794.
26. Yoon SS, Katz J, Brendel K, West KP Jr. Efficiency of EPI cluster sampling for assessing diarrhea and dysentery prevalence. *WHO Bull* 1997;75:417-426.

Books, Book Chapters, Monographs, Others

Caulfield LE. Interventions to increase dietary intakes of 6-12 month old infants in developing countries: what have we been able to accomplish? Linkages Working Paper, Academy for Educational Development (AED), Washington, DC, 1997.

Abstracts

Christian P, Schulze K, West KP, Khattry SK. Acute phase response among pregnant women with vitamin A deficiency related night blindness. *Experimental Biology '97, FASEB J* 1997;11:A614.

Christian P, West KP Jr, Katz J, Khattry SK, Kimbrough-Pradhan E, Shrestha SR, Pokhrel RP. The impact of vitamin A or beta-carotene supplementation on the incidence of night blindness during pregnancy and lactation in Nepal. XVIII IVACG Meeting, Cairo, Egypt 1997.

Craft, NE., S. Yamini, JH. Humphrey, ML. Dreyfuss, KP. West, Jr. 1997. Analysis of vitamin A in dried blood spots by HPLC. XVIII IVACG Meeting.

Dreyfuss ML, Stoltzfus RJ, Shrestha JB, Khattry SK, Shrestha SR, Pradhan EK, West KP Jr. Pregnancy anemia and neonatal weight in rural Nepal. *FASEB J* 1997;11:A654.

Dreyfuss ML, West KP Jr, Katz J, LeClerq SC, Pradhan EK, Adhikari RK, Stoltzfus RJ. Effects of maternal vitamin A or beta-carotene supplementation on intrauterine/neonatal and early infant growth in Nepal. XVIII IVACG Meeting, Cairo, 22-26 September, 1997.

Hadi H, Stoltzfus RJ, Dibley MJ, Moulton LH, West KP, Kjolhede CL, Sadjimini T. Vitamin A supplementation improves linear growth of Indonesian preschool children. XVIII IVACG Meeting, Cairo, 22-26 September, 1997.

Khattry SK, LeClerq SC, Adhikari RK, Amatya R, Pradhan EK, Dreyfuss ML, Katz J, Wu LS-F, Shrestha JB, West KP Jr. Effect of maternal vitamin A or beta-carotene supplementation on incidence of birth defects among Nepalese infants. XVIII IVACG Meeting, Cairo, Egypt 1997.

LeClerq SC, West KP Jr, Katz J, Khattry SK, Pradhan EK, Shrestha SR, Connor PB, Sommer A. Purpose, design, and methods of a double-masked, randomized community trial on the impact of maternal vitamin A or beta-carotene supplementation in Nepal. XVIII IVACG Meeting, Cairo, Egypt 1997.

Rice AL, Stoltzfus RJ, de Francisco A, Chakraborty J, Kjolhede CL, Wahed MA. Maternal vitamin A or beta-carotene supplementation in lactating Bangladeshi women: effects on mothers and infants. XVIII IVACG Meeting, Cairo, 22-26 September, 1997.

Shankar, A.H., B. Genton, S. Tamja, S. Arnold, L. Wu, M. Baisor, J. Paino, J.A. Tielsch, and M.A. Alpers. (1997). Zinc supplementation can reduce malaria-related morbidity in preschool children. *Am. J. Trop. Med. Hyg.* 57(3): A434.

Sibailly, T., SZ. Wiktor, ER. Ekpini, J. Bertolli, S. Yamini, KM. De Cock, GI. Adjorlolo, M. Laga, and A. Greenberg. 1997. Maternal vitamin A deficiency and mother-to-child transmission of HIV-1 in Abidjan, Cote-D'Ivoire. [Abstr B. 1174] Xth International Conference on AIDS and STD in Africa. December 7-11.

Stallings RY, Stoltzfus RJ, Schulze K, Miotti P. Negative association of an acute phase protein with maternal serum retinol in HIV infection. XVIII IVACG Meeting, Cairo, 22-26 September, 1997.

Selected Publications (1997)
Vitamin A for Health and Micronutrient for Health Cooperative Agreement
between The Johns Hopkins University and USAID

Stoltzfus RJ, Albonico M, Chwaya HM, Tielsch J, Savioli L. Impact of school-based deworming on stunting in Zanzibar. *FASEB J* 1997; 11:A574.

Stoltzfus RJ, Dreyfuss M, Shrestha JB, Khatri SK, Schulze K, West KP Jr. Effect of maternal vitamin A or beta-carotene supplementation on iron-deficiency anemia in Nepalese pregnant women, post-partum mothers, and infants. XVIII IVACG Meeting, Cairo, Egypt 1997.

West KP Jr, Khatri SK, Katz J, LeClerq SC, Pradhan EK, Shrestha SR, Connor PB, Dali S, Adhikari R, Pokhrel RP, Sommer A. Impact of weekly supplementation of women with vitamin A or beta-carotene on fetal, infant and maternal mortality in Nepal. XVIII IVACG Meeting, Cairo, Egypt 1997.

Yamini, S., KP. West, Jr., R. Wyse, U. Weigand, SK. Khatri, ML. Dreyfuss, RJ. Stoltzfus 1997. Effect of maternal vitamin A or B-carotene supplementation on circulating retinoid levels in Nepalese women during pregnancy and lactation. XVIII IVACG Meeting. Cairo, Egypt

Yamini, S., L. Zhou, LSF. WU, D. Yang, ML. Dreyfuss, and KP. West Jr. Impact of B-carotene (BC) supplementation on circulating levels of retinol, tocopherols (toc) and other carotenoids in Nepalese women. *FASEB Journal*. 12(4) : A1244.

Zhou L-M, Yang, W-W, Hua J-A, Deng C-O, Tao X, Stoltzfus RJ. Hemoglobin concentration in early pregnancy and preterm birth. *FASEB J* 1997; 11:A654.

APPENDIX 3

**LIST OF 1998 PUBLICATIONS
(January-September, 1998)**

1998 Publications (Jan-Sept)

Peer-reviewed Journal Articles (published or in press)

Vitamin A

1. Choi JK, Akib A, Munasir Z, Permaesih, Komala, Muherdiyantiningsih, Martuti S, Muhilal, Semba RD. Effects of vitamin A supplementation with measles vaccine on lymphocyte subsets in young infants. *J Nutr Immunology* 1998 (in press).
2. Christian P, West KP Jr, Khattry SK, Katz J, LeClerq S, Pradhan EK, Shrestha SR. The impact of low dose maternal vitamin A or beta-carotene on night blindness during pregnancy and the postpartum period in Nepal. *J Nutr* 1998 (in press).
3. Christian P, West KP Jr, Khattry SK, Katz J, LeClerq SC, Pradhan Ek, Shrestha SR. Vitamin A or B-carotene supplementation reduces but does not eliminate maternal night blindness in Nepal. *J Nutr* 1998;128:1458-1463.
4. Christian P, West KP Jr., Khattry SK, Katz J, Shrestha SR, Pradhan EK, LeClerq SC, Pokhrel RP. Night blindness of pregnancy in rural Nepal - nutritional and health risks. *Int J Epidemiol* 1998;27:231-137.
5. Christian P, Schulze K, Stoltzfus RJ, West KP Jr. Hyporetinolemia, illness symptoms, and acute phase protein response in pregnant women with and without night blindness. *Am J Clin Nutr* 1998;67:1237-1243.
6. Christian P, Bentley ME, Pradhan R, West KP, Jr. An ethnographic study of night blindness 'ratauni' among women in the terai of Nepal. *Soc Sci Med* 1998;46:879-889.
7. Christian P, Thorne-Lyman AL, West KP Jr., Bentley ME, Khattry SK, Pradhan EK, LeClerq SC, Shrestha SR. Working after the sun goes down: Exploring how night blindness impairs women's work activities in rural Nepal. *Eur J Clin Nutr* 1998;52:519-524.
8. Gittelsohn J, Shankar AV, West KP Jr., Faroukh F, Gnywali T, Pradhan.E. Child feeding and care behaviors are associated with xerophthalmia in rural Nepalese households. *Soc Sci Med* 1998;47:477-486.
9. Khattry SK, Shrestha SR, LeClerq S, Pradhan EK, Christian P, West KP. Maternal night blindness in Nepal: health risks and consequences. *J Nepal Med Assoc* 1998;37:427-433.
10. Humphrey JH, Agoestina T, Wu L, Juliana A, Septiana S, Ichord RN, Widjaja H, Cerreto M, Katz J, West KP Jr. Neonatal vitamin A supplementation: effect on development and growth at 3 years of age. *Am J Clin Nutr* 1998;68:109-117.
11. Semba RD, Miotti PG, Chipangwi JD, Yang LP, Saah A, Hoover DR. Maternal vitamin A deficiency and infant mortality in Malawi. *J Trop Ped* 1998;44:232-234.
12. Semba RD. The role of vitamin A and related retinoids in immune function. *Nutr Rev* 1998;56:S38-S48.
13. Shankar AV, Gittelsohn J, West KP Jr., Stallings R, Gnywali T, Faruque F. "Eating from a shared plate affects food consumption in vitamin A deficient Nepali children. *J Nutr* 1998;128:1127-1133.

Selected Publications (Jan-Sept 1998)
Vitamin A for Health and Micronutrient for Health Cooperative Agreement
between The Johns Hopkins University and USAID

14. Shankar AV, Gittelsohn J, Pradhan EK, Dhungel C, West KP Jr. Home gardening and access to animals in households with xerophthalmic children in rural Nepal. *Food Nutr Bull* 1998;19:34-41.
15. Shankar AV, Gittelsohn J, Pradhan R, Dahal B, West K Jr. Night blindness, diet and health in Nepalese children: An ethno-epidemiological investigation of local beliefs. *Ecol Food Nutr* (in press).
16. Sommer A. Moving from science to public health programs: lessons from vitamin A. *Am J Clin Nutr* 1998;68:513S-516S.
17. Sommer A. Xerophthalmia and vitamin A status. *Progress in Retinal and Eye Research* 1998;17:9-31.

Vitamin A and HIV

18. Semba RD, Lyles CM, Margolick J, Caiaffa WT, Farzadegan H, Cohn S, Vlahov D. Vitamin A supplementation and human immunodeficiency virus load in injection drug users. *J Infectious Diseases* 1998;177:611-616.
19. Semba RD, Miotti PG, Lan Y, Chiphangwi JD, Hoover DR, Dallabetta GA, Yang LP, Saah AJ. Maternal serum lactoferrin and vertical transmission of HIV. *AIDS* 1998;12:331-332.
20. Semba RD, Bulterys M, Graham NMH, Chan DW, Chao A, Flynn C, Saah A, Dushimimana A. Maternal micronutrient deficiencies and mother-to-child transmission of human immunodeficiency virus in Rwanda. *J Acquired Immune Deficiency Syndromes and Human Retrovirology*. (Provisionally accepted).
21. Semba RD. Micronutrients and the pathogenesis of HIV/AIDS. Proceedings of the 16th International Congress of Nutrition. July 27-August 1, 1997, Montreal, Canadian Federation of Biological Sciences. (in press).
22. Semba RD, Tang AM. Micronutrients and the pathogenesis of HIV infection. *Brit J Nutr* (in press).

Vitamin A and Malaria

23. Lewallen S, Taylor TE, Molyneux ME, Semba RD, Wills BA, Courtright P. Association between measures of vitamin A and the ocular fundus findings in cerebral malaria. *Arch Ophthalmol* 1998;116:293-296.

Iron Deficiency and Anemia

24. Albonico M, Stoltzfus RJ, Cancrini G, Tielsch JM, Chwaya HM, Ercole E, Savioli L. Epidemiological evidence for a differential effect of hookworm species, *A. duodenale* or *N. americanus*, on iron status of children. *Int J Epidemiol* 1998;27:530-537.
25. O'Brien KO, Zavaleta N, Caulfield LE, Yang DX, Abrams SA. The influence of prenatal iron and zinc supplement on absorption of supplemental iron, red blood cell incorporation and iron status in pregnant Peruvian women. *Am J Clin Nutr* 1998 (in press).
26. Christian P. Antenatal iron supplementation as a child survival strategy. Letter to the editor. *Am J Clin Nutr* 1998:404-405.
27. Stoltzfus RJ, Albonico M, Chwaya HN, Tielsch JM, Schulze KJ, Savioli L. Effects of the Zanzibar school-based deworming program on iron status of children. *Am J Clin Nutr* 1998;68:179-186.

28. Stoltzfus RJ, Chakraborty J, Rice A, de la Briere B, de Francisco A. Plausible evidence of effectiveness of an iron supplementation programme for pregnant and post-partum women in rural Bangladesh. *Food Nutr Bull* 1998;19:197-204.
29. Zhou LM, Yang W-W, Hua J-Z, Deng C-Q, Tao X, Stoltzfus RJ. Relation of hemoglobin measured at different times in pregnancy to preterm birth and low birth weight in Shanghai, China. *Am J Epidemiol* (accepted).

Zinc Deficiency

30. Caulfield LE, Zavaleta N, Shankar AH, Merialdi M. Potential contribution of maternal zinc supplementation during pregnancy to maternal and child survival. *Am J Clin Nutr* 1998;68:499S-508S.
31. Caulfield LE, Zavaleta N, Rivera K. Adding zinc to prenatal iron and folate supplements improves maternal and neonatal zinc status in a Peruvian population. *Am J Clin Nutr* (in press).
32. Christian PS, West KP Jr. Interactions between zinc and vitamin A: An update. *Am J Clin Nutr* 1998;68:435S-441S.
33. Merialdi M, Caulfield LE, Zavaleta N, Figueroa A, DiPietro J. Adding zinc to prenatal iron and folate supplements improves fetal neurobehavioral development. *Am J Obstet Gynecol* 1998 (in press).
34. Shankar AH, Prasad AA. Zinc and immune function: the biological basis of altered resistance to infection. *Am J Clin Nutr*. (in press).

Iodine Deficiency

35. Taffs RE, Enterline JC, Rusmil K, Muhilal, Suwardi SS, Rustama D, Djatnika, Cobra C, Semba RD, Cohen N, Asher DM. Oral iodine supplementation does not reduce neutralizing-antibody responses to oral poliovirus vaccine. *Bull WHO* (provisionally accepted).

Other

36. Albonico M, Stoltzfus RJ, Savioli L, Chwaya HM, d'Harcourt E, Tielsch JM. A controlled evaluation of two school-based anthelmintic chemotherapy regimens on intensity of helminth infections. *Int J Epidemiol* (accepted for publication).
37. Caulfield LE, Stoltzfus RJ, Witter FR. Implications of the Institute of Medicine weight gain recommendations for preventing adverse pregnancy outcomes in black and white women. *Am J Pub Health* (accepted).
38. Caulfield LE, Huffman SL, Piwoz EG. Interventions to improve the intakes of complementary foods of 6-12 month old infants: impact on growth, prevalence of malnutrition and potential contribution of child Survival. *Food Nutr Bull* (in press).
39. Gittelsohn J, Mookherji S, Pelto G. Operationalizing Household Food Security in Rural Nepal. *Food Nutr Bull* (in press).
40. Goetghebeur E, Molenberghs G, Katz J. Estimating causal effect of compliance on binary outcome in randomized controlled trials. *Statistics in Medicine* 1998;17:341-355.

41. Katz J, West KP Jr, LeClerq SC, Thapa MD, Khatri SK, Pradhan EK, Shrestha SR, Pokhrel RP. Agreement between clinical examination and parental morbidity histories for children in Nepal. *J Trop Ped* 1998;44:225-229.
42. Navitsky RC, Dreyfuss ML, Shrestha J, Khatri SK, Stoltzfus RJ, Albonico M. *Ancylostoma duodenale* is responsible for hookworm infections among pregnant women in the rural plains of Nepal. *J Parasitol* 1998;84:647-651.
43. Park SW, Royal W, Semba RD, Wiegand GW, Griffin DE. Expression of adhesion molecules and CD28 on T lymphocytes during human immunodeficiency virus infection. *Clinical and Diagnostic Laboratory Immunology* 1998;5:583-587.

Books, Book Chapters, Monographs, Others

1. Stoltzfus RJ, Dreyfuss ML. Program guidelines for the control of iron deficiency anemia. International Nutritional Anemia Consultative Group (INACG), 1998.
2. Stoltzfus RJ. The impact of parasitic infections on nutrition. In: Hunters Tropical Medicine, 7th edition, Strickland GT, ed. WB Saunders Company: Orlando 1998 (in press).
3. West KP Jr, Christian P. Maternal night blindness: Extent and associated risk factors. IVACG Statement, International Vitamin A Consultative Group, Washington, DC, 1998.

Abstracts

1. Christian P, West KP Jr, Khatri SK, Katz J, LeClerq SC, Pradhan EK, Shrestha SR. The impact of vitamin A and beta-carotene supplementation on night blindness during pregnancy and lactation in Nepal. *FASEB J* 1998;12:A213.
2. Dreyfuss ML, Craft NE, Yamini S, Humphrey JH, West KP Jr. Vitamin A analysis in dried blood spots by HPLC. *FASEB J* 1998;12:A840.
3. Rice AL, Stoltzfus RJ, de Francisco A, Chakraborty J, Kjolhede CL, Wahed MA. Maternal vitamin A or beta-carotene supplementation in lactating Bangladeshi women: effects on mothers and infants. *Experimental Biology '98 meeting*, San Francisco, CA, Apr 18-22, 1998.
4. Schulze KJ, Gautschi LA, Dreyfuss ML, Wu LSF, West KP Jr. Urinary iodine during pregnancy and lactation in Nepali women. *FASEB J* 1998;12:A343.
5. Shankar, A.H., A. Gbakima, L. Caulfield, and N. Zavaleta. (1998) The influence of maternal zinc supplementation on immunological development of the neonate and perinatal morbidity. *FASEB J*. 12:A4741.
6. Shankar, AH, B. Genton, J. Taraika, A. Gbakima, R. Anders, R.D. Semba, J. Kazura and M Alpers (1998). The influence of vitamin A supplementation on malaria-specific cytokine responses in an endemic area. *FASEB summer conference on retinoids*. June 1998.
7. West KP Jr, Katz J, Khatri SK, LeClerq SC, Pradhan EK, Shrestha SR, Connor PB, Dali S, Adhikari R, Pokhrel RP, Sommer A. Weekly supplementation of women with vitamin A or beta-carotene lowers maternal mortality in Nepal. *FASEB J* 1998;12:A343.

APPENDIX 4

PROFESSIONAL SERVICES

Professional Services

Name	Service
Joanne Katz	<p>Journal Peer Reviews: American Journal of Epidemiology American Journal of Clinical Nutrition American Journal of Public Health, Controlled Clinical Trials Pediatric Infectious Disease, Archives of Ophthalmology Investigative Ophthalmology and Vision Sciences Ophthalmology</p> <p>Associate Editor American Journal of Epidemiology</p>
Anuraj Shankar	<p>Journal Peer Reviews: American Journal of Clinical Nutrition Journal of Immunology</p> <p>Scientific Review Panels: WHO ARCH</p> <p>Others: IVACG - Safety of Vitamin Linked to Immunizations INACG - Safety of Iron Supplements for Malaria Areas</p>
Laura Caulfield	<p>Journal Peer Reviews: Journal of Nutrition American Journal of Epidemiology American Journal of Clinical Nutrition International Journal of Epidemiology</p> <p>Scientific Review Panels: Thrasher USDA Nestle Foundation Earthwatch Foundation</p>

Keith P. West, Jr.	<p>Journal Peer Reviews: Acta Paediatrica American Journal of Clinical Nutrition American Journal of Epidemiology Archives of Ophthalmology Ecology of Food and Nutrition European Journal of Clinical Nutrition Journal of the American Medical Association Journal of Nutrition Maryland Medical Journal, Nutrition Research</p> <p>Scientific Review Panels Thrasher Research Fund Wellcome Trust</p> <p>Others: IVACG</p>
Jean Humphrey	<p>Journal Peer Reviews: International Journal of AIDs</p> <p>Other Thematic rapateour, IVACG meeting, Cairo</p>
Rebecca Stoltzfus	<p>Journal Peer Reviews: American Journal of Clinical Nutrition American Journal of Epidemiology European Journal of Clinical Nutrition Journal of Nutrition International Journal of Epidemiology National Medical Journal of India</p> <p>Scientific review panels: Thrasher Institute of Medicine</p> <p>Others: IVACG INACG OMNI MI UNICEF WHO</p>

APPENDIX 5

LECTURES

Lectures

Date	Title/Audience/Place	Person
10/97	Current topics in Nutrition/JHU/iron and Malaria	Anuraj Shankar
10/97	Recommendations for micronutrient interventions for adolescents and women of child-bearing age, SLAN, Guatemala City, Guatemala	Keith P. West, Jr.
10/97	Recommendations for micronutrient interventions for adolescents and women of child-bearing age, SLAN, Guatemala City, Guatemala	Laura Caulfield
11/14/97	'Vitamin A Deficiency: Impact on Health and Vision' at Helmut Horten Foundation, Zurich Switzerland	Alfred Sommer
11/20/97	'Vitamin A and Child Health' at Roche in Basle, Switzerland	Alfred Sommer
11/97	"Vitamin A deficiency in child and maternal health and survival: new findings." ILSI Brazil seminar "Enriching Lives Investing in Nutrition" in Sao Paulo, Brazil	Keith P. West, Jr.
12/1/97	"Dr. Sommer's Night blindness work" at JHU to undergraduate students	Alfred Sommer
12/9/97	"Pioneering work in Vitamin A" at Helen Keller International Board of Director's ceremony, NY	Alfred Sommer
12/97	Iron deficiency and anemia in Honduras, updating the recommendations for maternal interventions to reduce anemia in pregnancy. OMNI sponsored meeting, revising norms for integrated maternal-infant care, updating guidelines for iron supplementation for women during pregnancy, Tegucigalpa, Honduras	Laura Caulfield
12/97	Iron deficiency and anemia in Honduras, updating the recommendations for maternal interventions to reduce anemia in pregnancy. OMNI sponsored meeting, revising norms for integrated maternal-infant care, updating guidelines for iron supplementation for women during pregnancy, Tegucigalpa, Honduras	Keith P. West, Jr.
1/98	Vitamin A and Childhood Mortality and Morbidity lectures given at the Institute of Nutrition at Mahidol University	Alfred Sommer
2/11/98	Nutrition Surveys/JHU students/JHU	Joanne Katz
4/21/98	"Vitamin A-From Eyes to Lives", Royal College of Ophthalmologists Tenth Anniversary Congress, Glasgow, Scotland	Alfred Sommer
5/5/98	Lecture given to internists from around the US at a Clinical Medicine Course, JHU	Alfred Sommer
5/6-7/98	Potential benefits of iron supplementation during pregnancy for maternal and infant health, PVO/Core Group, Washington, DC	Laura Caulfield
5/6-7/98	"Vitamin A supplementation guidelines, assessments and indicators." "The Path to Maternal and Child Health: The PVO Role in Improving Iron and Vitamin A Status" Conference, The CORE Group, PAHO, Washington, DC	Keith P. West, Jr.
5/6-7/98	"Vitamin A supplementation in pregnant women - biology & benefits." "The Path to Maternal and Child Health: The PVO Role in Improving Iron and Vitamin A Status" Conference, The CORE Group, PAHO, Washington, DC	Keith P. West, Jr.
5/98	Potential benefits of iron supplementation during pregnancy for maternal and infant health, PVO/Core Group, Washington, DC	Keith P. West, Jr.
5/18/98	Impact of vitamin A and B-carotene supplementation of women in reducing pregnancy-related mortality: a randomized double-masked community trial in Nepal," Harvard Nutrition Seminar Series, Harvard School of Public	Keith P. West, Jr.

	Health, Cambridge, MA.	
5/25-28/98	Vitamin A Supplementation: Impact on Morbidity and Mortality. An Update. (Plenary Talk). Presented at the Nutrition Congress of South Africa, Johannesburg, South Africa ; and Neonatal Vitamin A Supplementation during Micronutrient symposium: Nutrition congress of South Africa, Johannesburg, SA	Jean Humphrey
5/27/98	"Vitamin A Deficiency as a Public Health Problem" lecture given at Johns Hopkins Hospital Pediatric Grand Rounds	Alfred Sommer
5/28/98	"New Imperatives for an Old Vitamin: Prevention of Blindness for Pennies", University of Iowas Hospital and Clinics, Iowa City, Iowa	Alfred Sommer
6/11/98	Sample size issues in community trials course on "Clinical Trials: Design, Analysis and Dissemination of Results"	Joanne Katz
6/21/98	"Vitamin A Deficiency and Xerophthalmia: Past, Present and Future" at Scientific Symposium of XXVIIIth Meeting of Academia Ophthalmologica Internationalis, Amsterdam, The Netherlands	Alfred Sommer
6/22/98	Vitamin A and EPI: Review of the Optimal dose of vitamin A to be administered at EPI visits	Keith P. West, Jr.
6/24/98	"Taking Stock: An international score card: Glaucoma, Cataract and Xerophthalmia", Prevention of Blindness Session of the International Council of Ophthalmology. The Netherlands	Alfred Sommer
6/24/98	The Rise and Fall of Vitamin A as Anti-Infective Therapy, 1920-1940; National Library of Medicine, Seminar in the History of Medicine	Richard D. Semba
6/98	Summer Institute for Tropical Medicine/JHU/Immunology	Anuraj Shankar
7/28/98	Vitamin A SOTA Course: ""The Science"", Washington, DC	Keith P. West, Jr.
7/98	Summer Institute for Tropical Medicine/JHU/Immunity to Malaria	Anuraj Shankar
8/98	International Health/Micronutrients and Immunity/Case Western Reserve University	Anuraj Shankar
8/98	Maternal zinc supplementation during pregnancy and infant health, International Zinc Conference, Lima, Peru	Laura Caulfield
8/10/98	Tropical medicine Course at JHSPH "Global Blindness"	Joanne Katz
9/5-18/98	"Vitamin A deficiency: an underlying determinant of child and maternal mortality in the third world." Second European Congress on Tropical Medicine, Liverpool, UK.	Keith P. West, Jr.

APPENDIX 6

MEETINGS

Meetings

Date	Place	Purpose	Person
10/14/97	USAID, Washington, DC	Maternal Health & Survival Strategic Objective Meeting	Keith P. West, Jr.
10/16-17/98	Arlington, Va	OMNI Strategic Planning Meeting	Keith P. West, Jr.
12/8/98	Arlington, Va	OMNI Strategic Planning Meeting	Keith P. West, Jr.
12/12/98	Johns Hopkins University	Meeting re MHCA with USAID	Keith P. West, Jr.
3/6/98	American Red Cross, Washington, DC	Overview of USAID Enhanced Vitamin A Effort (VITA)	Keith P. West, Jr.
3/11/98	Washington, D.C.	IVACG Steering Committee	Keith P. West, Jr.
3/12-13/98	ILSI, Washington, DC	Simplified Dietary Assessment Methods Workshop	Keith P. West, Jr.
4/18-22/98	San Francisco	Experimental Biology Meeting	Keith P. West, Jr.
4/29/98	Arlington, Va	OMNI Strategic Planning Meeting	Keith P. West, Jr.
5/5-6/98	Washington, DC	CORE Group Meeting	Keith P. West, Jr. Laura Caulfield
5/8/98	USAID, Washington, DC	Meeting with USAID	Keith P. West, Jr.
6/11-12/98	Paris, France	International Symposium on Nutrition and Pregnancy	Parul Christian
6/12/98	Arlington, Va	OMNI Strategic Planning Meeting	Keith P. West, Jr.
7/6-7/98	Washington, DC	"Iron and Maternal Mortality in the Developing World", OMNI-Research, ILSI	Keith West
7/28/98	USAID, Washington, DC	Meeting with USAID	Keith P. West, Jr.

APPENDIX 7

TECHNICAL ASSISTANCE

Technical Assistance

Date(s)	Agency or Individual to whom TA was provided/ and Purpose of TA	Person
10/97	Provided training on dark adaptometry	Nathan Congdon
10/18-19/97	UNICEF, New York. "State of the World's Children"	Keith P. West, Jr.
12/98	OMNI, to advise the MOH on the new INACG recommendations for iron supplementation during pregnancy	Laura Caulfield
12/17-18/97	UNICEF Consultancy on VA program enhanced effort, NY	Al Sommer Keith P. West, Jr.
1/98	Developed and sent questions on maternal night blindness for Dr. Meera Shekar, UNICEF/Philippines	Keith P. West, Jr. Parul Christian
3/98 to 9/98 (various points)	TA to revise the questionnaires for the next phase of DHS surveys, specifically on infant feeding, maternal health, maternal facilities questionnaires, nutrition component on anthropometry, micronutrient status.	Laura Caulfield
5/5-7/98	Presentations on Improving iron and VA status given to the CORE Group	Keith P. West, Jr.
5/29/98	Response to TA request from Jere Douglas Hass re multiple micronutrient intervention to lactating women and non-lactating pregnant women	Keith P. West, Jr.
5/30/98	Response to TA request from HKI/Bangladesh re fortification of food aid product with VA	
6/12-16/98	Training of Thai colleagues in techniques of dark adaptation, planning of dark adaptation study	Nathan Congdon
7/9/98	Provided technical update on micronutrients for Save the Children technical staff, Westport, Connecticut	Keith P. West, Jr.
7/15-16/98	Provided consultation to Indonesian team on development of a community eye care program in Indonesia (Prof. Mandang-Member of Parliament; Farida Sirla-Head of Subdirector Community Eye Health, MOH; Durban Ardjo-Sight first Project, Lions)	James Tielsch Joanne Katz Keith West
7/98	Served as a reviewer in the FAO/WHO Joint Expert Consultation on Human vitamin and Mineral Requirements	Keith P. West, Jr.
8/98	TA for VA and growth analysis	H. Haddi
8/20/98	Vision and Vitamin A, JHU Summer Course	Alfred Sommer
8/98	Najat Mokhtar, Assistance with data analysis and drafting report on vitamin A results for women and children in Morocco;	Keith P. West, Jr. Anita Shankar Essie Yamani Rebecca Stoltzfus
9/16-17/98	Chaired two-day meeting of IVACG Steering Committee, Washington, D.C.	Alfred Sommer

APPENDIX 8

TRAVEL

Travel

Dates	Country	Person	Purpose
10/97	Guatemala	Laura Caulfield	Attend SLAN
11/24/97-12/9/97	Madurai, India	Jim Tielsch	Provide TA to VASIN study
1/98	Kathmandu, Nepal	Al Sommer Keith P. West, Jr. Jim Tielsch Joanne Katz Parul Chritian Nepalese colleagues	Participate in NNIPS-2 annual convention; monitor NNIPS-2 activities; initiate NNIPS-3 plans.
1/19/98-2/11/98	Madurai, India	Jim Tielsch	Provide TA to VASIN study
2/98	India	Al Sommer Keith P. West, Jr. Joanne Katz Parul Chritian	Explore potential study sites for replicate maternal supplementation trial. Give mini-symposium for Nutrition Society of India on NNIPS-2 at UNICEF/USAID request.
5/25/98-5/28/98	Johanesburg, South Africa	Jean Humphrey	Present at Nutrition Congress of South Africa
6/12/98-6/16/98	Bangkok, Thailand	Nathan Congdon	Train INMU colleagues in dark adaptometry and study design.
7/22/98-7/30/98	Baltimore, MD	Jean Humphrey	Prepare proposal for Infant Feeding in the context of HIV
7/31/98-8/31/98	Kathmandu, Nepal		Visit NNIPS project
9/14/97-9/26/97	Madurai, India	Jim Tielsch	Provide TA to VASIN study