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**Report of the**

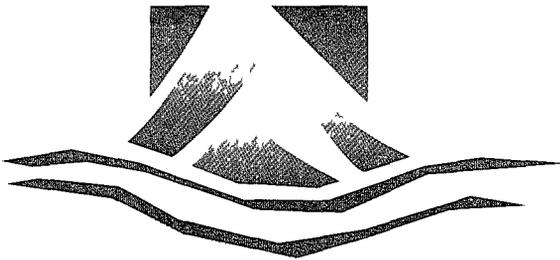
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**XVII International Vitamin A**

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**Consultative Group Meeting**

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**Virtual Elimination  
of Vitamin A  
Deficiency:  
Obstacles and  
Solutions for the  
Year 2000**

**Guatemala City, Guatemala**

**18-22 March 1996**

**T**he mission of the International Vitamin A Consultative Group (IVACG) is to guide international activities aimed at reducing vitamin A deficiency in the world. The group offers consultation and guidance to various operating and donor agencies that are seeking to reduce vitamin A deficiency and its accompanying blindness. As part of this service, IVACG has prepared guidelines and recommendations for

- ◆ assessing the regional distribution and magnitude of vitamin A deficiency,
- ◆ developing intervention strategies and methodologies to control vitamin A deficiency,
- ◆ evaluating the effectiveness of implemented programs on a continuing basis, and
- ◆ undertaking research needed to support the assessment, intervention, and evaluation of programs

#### **IVACG has published the following monographs**

- ◆ *Guidelines for the Eradication of Vitamin A Deficiency and Xerophthalmia* (1977)
- ◆ *Recent Advances in the Metabolism and Function of Vitamin A and Their Relationship to Applied Nutrition* (1979)
- ◆ *The Safe Use of Vitamin A* (1980) (Available in English and French)\*
- ◆ *The Symptoms and Signs of Vitamin A Deficiency and Their Relationship to Applied Nutrition* (1981) (Available in Spanish only)\*
- ◆ *Biochemical Methodology for the Assessment of Vitamin A Status* (1982)\*
- ◆ *Reprints of Selected Methods for the Analysis of Vitamin A and Carotenoids in Nutrition Surveys* (1982)\*
- ◆ *Periodic, Large Oral Doses of Vitamin A for the Prevention of Vitamin A Deficiency and Xerophthalmia: A Summary of Experiences* (1984)
- ◆ *A Decade of Achievement: The International Vitamin A Consultative Group (IVACG) 1975-1985* (1987)
- ◆ *The Safe Use of Vitamin A by Women During the Reproductive Years* (1986) (Available in English and French)\*
- ◆ *Biochemical Methodology for the Assessment of Carotenes* (1987)
- ◆ *Guidelines for the Use of Vitamin A in Emergency and Relief Operations* (1988) (Available in French only)\*
- ◆ *Vitamin A Supplements: A Guide to Their Use in the Treatment and Prevention of Vitamin A Deficiency and Xerophthalmia* (published by the World Health Organization in conjunction with IVACG and UNICEF, 1988, new edition in press)\*
- ◆ *Guidelines for the Development of a Simplified Dietary Assessment to Identify Groups at Risk for Inadequate Intake of Vitamin A* (1989)
- ◆ *Methodologies for Monitoring and Evaluating Vitamin A Deficiency Intervention Programs* (1989)\*
- ◆ *Nutrition Communications in Vitamin A Programs: A Resource Book* (1992)\*
- ◆ *A Brief Guide to Current Methods of Assessing Vitamin A Status* (1993)\*
- ◆ *IVACG Statement on Clustering of Xerophthalmia and Vitamin A Deficiency Within Communities and Families* (1996)\*
- ◆ *IVACG Policy Statement on Vitamin A, Diarrhea, and Measles* (1996)\*
- ◆ *Strategic Placement of IVACG in the Evolving Micronutrient Field* (1996)\*\*

\* These reports are available free of charge to developing countries and for US\$3 50 to developed countries. Copies can be ordered from the IVACG Secretariat.

\*\* This report is available free of charge.





## **IVACG Steering Committee**

Moses Chirambo, M D  
Frances R Davidson, Ph D ,  
IVACG Secretary  
Abraham Horwitz, M D , M P H ,  
IVACG Chair  
Vinodini Reddy, M D , D C H , FIAP  
Leonor Maria Pacheco Santos, Ph D  
Suttalak Smitasiri, Ph D  
Alfred Sommer, M D , M H Sc ,  
IVACG Steering Committee Chair  
Barbara A Underwood, Ph D  
Keith P West, Jr , Dr PH

## **XVII IVACG Meeting Rapporteurs**

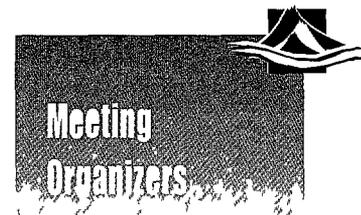
Emorn Wasantwisut, Ph D  
Anna Coutsooudis, Ph D

## **IVACG Secretariat**

Laurie Lindsay Aomari, R D  
Diane Dalsera, M B A  
Maribel Flewitt  
Suzanne S Harris, Ph D  
Dwayne Milbrand

## **Local Organizing Committee in Guatemala**

Dr Hernan L Delgado, Coordinator  
Instituto de Nutricion de Centro America y  
Panama  
Ministerio de Salud Publica y Asistencia  
Social  
Asociacion de Azucareros de Guatemala  
CeSSIAM  
Comite Prociegos y Sordos de Guatemala  
Fundacion Internacional del Ojo  
Oficina Panamericana de la Salud  
Proyecto HOPE  
Proyecto Salud Materno-Infantil  
Comunidad Economica Europea  
Programa Mundial de Alimentos  
UNICEF  
USAID



**M**any organizations and individuals contributed to the success of the XVII IVACG Meeting. IVACG Steering Committee members Dr. Moses Chirambo, Dr. Frances R. Davidson, Dr. Abraham Horwitz, Dr. Vinodini Reddy, Dr. Leonor Maria Pacheco Santos, Dr. Suttalak Smitasiri, Dr. Alfred Sommer, Dr. Barbara A. Underwood, and Dr. Keith P. West, Jr. gave of their energy and expertise to develop the meeting program. They carefully considered the scientific dimensions of the program in relation to the needs of colleagues in developing countries.

The secretariat relied on the wise counsel and generosity of the local organizing committee for the meeting, which was coordinated by Dr. Hernan Delgado at INCAP. Dr. Edmundo Alvarez, Ing. Leonel Anleu, Ms. Cecilia Z. de Arenas, Dr. Gustavo Bergonzoli, Dr. Jorge Bran, Dr. Jesus Bulux, Dr. Victor Calderon, Lic. Carmen Dardano, Dr. Omar Dary, Dr. Miguel Rene Escobar, Lic. Magda Fischer, Dr. Juan Carlos Garcia, Dr. Edgar Lara, Dr. Baudilio Lopez, Dr. Manolo Mazariegos, Lic. Ramon Mendoza, Lic. Veronika de Palma, Sra. Martha Burdick de Piedrasanta, Dr. Francisco Pineda, Lic. Francisco Puac, Lic. Nicté Ramirez, Ing. Ricardo Rojas, Lic. Eugenia Saenz de Tejada, Dr. Hector Emilio Soto Rodas, and Lic. Christa de Valverde worked continuously to strengthen and complement the meeting with regional presentations, special events, and local arrangements. The organizations contributing to the local committee and the many talented individuals representing these organizations were gifted hosts.

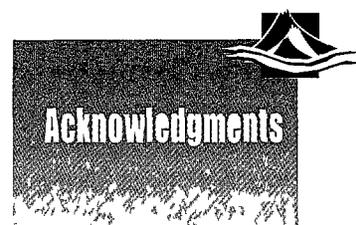
The IVACG Secretariat acknowledges the vital contributions of many groups in Guatemala, especially Productos Roche, S.A., Instituto de Nutricion de Centro America y Panama (INCAP), H. B. Fuller de Centroamerica, S.A., Kellogg de Centroamerica, S.A., BASF de Guatemala, S.A., PLATA/VISA, Cerveceria Centroamericana, S.A., Hotel Camino Real, Productos Nestle, S.A., Asociacion de Azucareros de Guatemala, D. H. L. de Guatemala, ANACAFE-Departamento de

Accion Social, Fabrica de Productos Lacteos Parma, Comité Prociegos y Sordos de Guatemala, INCAPARINA, INGUAT, Banco Agrícola Mercantil, CEMACO, BIC de Guatemala, Asociacion Hospicio de Occidente, Universidad del Valle, Ministerio de Cultura y Deportes, Ministerio de la Defensa, and Ministerio de Gobernacion.

Much of the meeting was organized with funding from Opportunities for Micronutrient Interventions (OMNI), a project of the Office of Health and Nutrition, Global Bureau for Programs, Field Support and Research, U.S. Agency for International Development. The IVACG Secretariat gratefully acknowledges the additional generous support of the Australian Agency for International Development (AusAID), The Coca-Cola Company, Heinz Institute of Nutritional Sciences, Inc., The Micronutrient Initiative Secretariat, Nestle S.A., The Procter & Gamble Company (USA), and Task Force SIGHT AND LIFE.

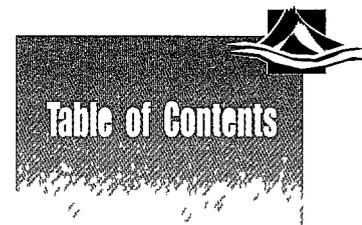
Dr. Emorn Wasantwisut and Dr. Anna Coutsoudis, overall rapporteurs for this meeting, had the daunting task of drafting a permanent record of the presentations and discussions. They were skillfully assisted by the meeting's thematic rapporteurs, Dr. Jean Humphrey, Ms. Victoria Sheffield, and Dr. Greg Hussey, and by the rapporteurs of the meeting's concurrent sessions, Dr. Venkatesh Mannar, Dr. Greg Hussey, Dr. Martin Bloem, Dr. Keith P. West, Dr. Penelope Nestel, Mr. David Alnwick, and Dr. Jean Humphrey. Readers worldwide will benefit from the efforts of this group. The secretariat is also grateful for the leadership and flexibility of the many chairpersons during program sessions.

Ing. Marco Tulio Sosa Ramirez, Guatemala's Minister of Public Health and Social Welfare, and the local organizing committee inaugurated the meeting and graciously welcomed us to Guatemala City during festive opening-night cultural events and a memorable fiesta at the end of the week. Refreshments during these events were generously provided by the meeting's





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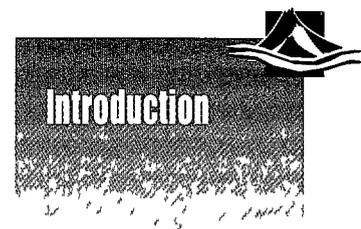
• AIDS	acquired immunodeficiency syndrome
DPT	diphtheria-pertussis-tetanus
EPI	Expanded Programme on Immunization
FFQ	food frequency questionnaire
HIV	human immunodeficiency virus
HKI	Helen Keller International
IEC	information, education, and communication
INCAP	Institute of Nutrition of Central America and Panama
• IU	international units
• IUGR	intrauterine growth retardation
IVACG	International Vitamin A Consultative Group
MRDR	modified relative dose-response
MSG	monosodium glutamate
NGO	nongovernmental organization
RBP	retinol-binding protein
RDR	relative dose-response
SD	standard deviation
USAID	United States Agency for International Development
VAD	vitamin A deficiency
WHO	World Health Organization

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The International Vitamin A Consultative Group (IVACG) is an organization dedicated to reducing the prevalence of vitamin A deficiency worldwide. Established in 1975 with support from the U.S. Agency for International Development, IVACG continues to analyze issues related to the etiology, treatment, and prevention of vitamin A deficiency. IVACG activities involve scientists, program planners, and policy makers throughout the world. Through its international meetings, IVACG provides a forum for new ideas, encourages innovations, recognizes important research findings, increases awareness of the latest survey data, and promotes action programs.



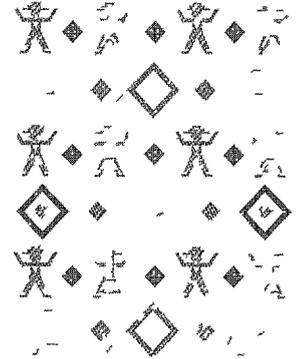
Representatives from 65 countries were among the 488 policy makers, program managers, planners, and scientists in health, nutrition, biochemistry, agriculture, horticulture, education, communications, and development who participated in the XVII IVACG Meeting, 18–22 March 1996 in Guatemala City, Guatemala. Throughout the five-day program, 130 presentations elucidated the meeting theme, “Virtual Elimination of Vitamin A Deficiency: Obstacles and Solutions for the Year 2000.” Numerous speakers presented research and programmatic information on implementing effective programs. Participants had the opportunity to share perspectives during interest group discussions and social events, review and order materials from 13 exhibits, and join postmeeting study tours. This report attempts to convey much of the material presented and some of the discussion that followed.

With growing international interest in the control of vitamin A deficiency and its role in child survival programs, the prevention and control of vitamin A deficiency has become a “mainline” health and nutrition activity. Indeed, prevention and control of vitamin A deficiency is now regarded as an integral component of an emerging strategy to integrate diverse efforts to increase child survival by controlling micronutrient deficiencies. Advocacy at all levels and direct interventions are still required. Both should be suited to the particular local conditions and resources in each country. According to Dr. Abraham Horwitz, IVACG chair, “There are distinct obstacles to preventing and controlling vitamin A deficiency. These should not deter but stimulate the identification of solutions to overcome them.”

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# Program





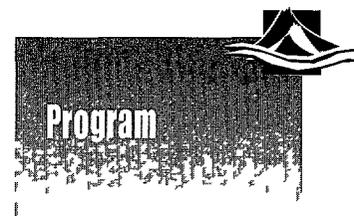
<b>Monday 18 March</b>	<b>Tuesday 19 March</b>	<b>Wednesday 20 March</b>	<b>Thursday 21 March</b>	<b>Friday 22 March</b>
0730 Registration	0800 Registration 0830 Exhibits open	0800 Registration	0800 Registration	0800 Registration
0800–1030 Plenary Session <b>Inaugural Ceremony</b>	0830–1000 Plenary Session <b>Micronutrient Forum</b>  <b>Bioavailability of Dietary Carotenoids</b>	0830–1030 Concurrent Sessions <b>1) Dietary Interventions</b> <b>2) Biologic Significance of Vitamin A Deficiency Growth and Inflammation</b>	0830–1030 Plenary Session <b>Summaries from Wednesday Concurrent Sessions</b>	0830–1000 Plenary Session <b>Summaries from Thursday Concurrent Sessions</b>
1030–1100 Poster Session	1000–1100 Poster Session	1030–1130 Poster Session	1030–1130 Poster Session	1000–1030 Break
1100–1230 Plenary Session <b>Actions for the Prevention and Control of Vitamin A Deficiency in Central America</b>	1100–1230 Plenary Session <b>Vitamin A Fortification of Foods</b>	1130–1330 Lunch Break	1130–1300 Plenary Session <b>Developing Sustainable Solutions for the Problem of Vitamin A Deficiency</b>	1030–1200 Plenary Session <b>Reports from Thematic Rapporteurs and Closing Remarks</b>
1230–1430 Lunch Break	1230–1430 Lunch Break		1300–1500 Lunch Break	1200 Adjournment
1430–1745 Plenary Session <b>Virtual Elimination of Vitamin A Deficiency Obstacles and Solutions for the Year 2000</b>	1430–1630 Concurrent Sessions <b>1) Experiences with Vitamin A Fortification of Foods</b> <b>2) Biologic Significance of Vitamin A Deficiency Infection</b>	1330–1630 Plenary Session <b>Summaries from Tuesday Concurrent Sessions</b>  <b>Using Ethnographic Methods in Vitamin A Deficiency Research</b>	1500–1730 Concurrent Sessions <b>1) Other Interventions for Prevention and Control of Vitamin A Deficiency</b> <b>2) Vitamin A Status Methodology</b>	<b>Saturday and Sunday, 23–24 March</b>  <b>Study Tours</b>  Sugar Fortification and Production of Fortified Foods (Guatemala City and Pacific Lowlands)
1600–1630 Poster Session				
1745 Meetings Adjourn	1630 Meetings Adjourn	1630 Meetings Adjourn	1715 Meetings Adjourn	
1830–2130 Welcome Reception	1700–1900 Interest Groups	1700–1830 Interest Groups 1700–1900 Video Session 2000–2130 Interest Groups	2000 Fiesta	Actions of Project Hope in the Western Highlands  Vitamin A for Child Survival Program in Coban

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## Sunday, 17 March

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- 0800–1300 IVACG Steering Committee Meeting
- 1700–1800 Set up for Monday's poster sessions  
Prevention and Control of Vitamin A Deficiency in  
Central America  
Surveys
- 1830–2030 Early Registration at Hotel Camino Real Guatemala



## Monday, 18 March

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- 0730 **Registration continues at Hotel Camino Real Guatemala**
- 0815 Guests and participants are seated
- Inaugural Ceremony**
- 0830 National Anthem
- 0845 Greeting from Master of Ceremonies  
Dr Omar Dary
- 0855 Message from the Chairman of the International Vitamin A Consultative  
Group (IVACG)  
Dr Abraham Horwitz
- 0905 Message from the Coordinator of the Local Committee of the XVII  
IVACG Meeting and Awards to guests of honor, Ms Elisa Molina de  
Stahl and Dr Guillermo Arroyave  
Dr Hernan L Delgado
- 0915 Message from the Director of the Pan American Health Organization  
Dr George A O Alleyne
- 0935 Opening address by the Minister of Public Health and Social Welfare of  
Guatemala  
Ing Marco Tulio Sosa Ramirez
- 1030 *Break and poster session with presenters available*  
**Prevention and Control of Vitamin A Deficiency in  
Central America**
- 1100 **Actions for the Prevention and Control of Vitamin A Deficiency in  
Central America**  
Moderator Dr Gustavo Hernandez Polanco
- 1100 Present Status of Vitamin A Deficiency in Central America  
Dr Jesus Bulux

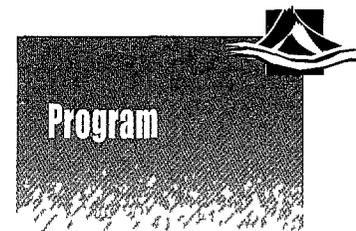


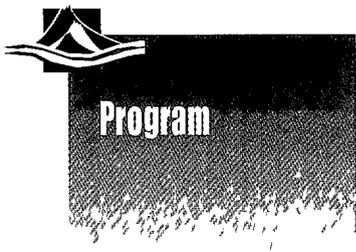
- 1130 Prevention and Control of Vitamin A Deficiency in Central America
  - Director General Minister of Health, Belize, Dr Jose Lopez
  - Director, Nutrition Department, Ministry of Health, Costa Rica,
  - Dra Rosa Novygrodt
  - Minister of Health, El Salvador, Dr Eduardo Interiano
  - Viceminister of Public Health and Social Welfare, Guatemala,
  - Dr Carlos Andrade
  - Viceminister of Health, Honduras, Dra Virginia Espinoza
  - Minister of Health, Nicaragua, Dr Federico Muñoz
  - Director General of Health, Panama, Dr Jorge Montalvan
- 1230 *Lunch*
- 1430 **Virtual Elimination of Vitamin A Deficiency Obstacles and Solutions for the Year 2000**
  - Moderator Dr Alfred Sommer
- 1430 Presentation of the meeting theme
  - Dr Abraham Horwitz
- 1440 Present Status and Global Progress Toward the Year 2000 Goal
  - Dr Barbara A Underwood
- 1500 Obstacles and Solutions to Reaching the Year 2000 Goal of Control of Vitamin A Deficiency
  - India Dr Vinodini Reddy
  - Ghana Mrs Rosanna Agble
  - Tanzania Dr Godwin Ndossi
  - Indonesia Dr Martin Bloem
- 1600 *Break and poster session with presenters available*
- Surveys**
- 1630 Response Panel
  - Bolivia Dra Maria del Carmen de Daroca
  - Nepal Mr Ram K Shrestha
  - Vietnam Prof Ha Huy Khoi
  - Ghana Dr Paul Arthur
- 1730 Response of the U S Agency for International Development to the Global Challenge of Vitamin A Deficiency
  - Dr Nils Daulaire
- 1745 End of day's formal sessions
  - Set up for Tuesday's poster sessions
  - Micronutrient Interactions
  - Experiences with Vitamin A Fortification of Foods
  - Biologic Significance of Vitamin A Deficiency Infection
- 1830 Buses depart for welcome reception
- 1900–2130 **Welcome reception at Museo de la Cerveceria Centroamericana, S A**
  - Hosts Local Committee XVII IVACG Meeting and
  - Cerveceria Centroamericana, S A

**Tuesday, 19 March**

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- 0800 Set up for exhibits
- 0830 **Exhibits open**
- 0830 **Micronutrient Forum**  
Chair Dr Frances R Davidson
- 0835 Interaction of Micronutrients to Build Pre-pregnancy Iron Reserves in Adolescent Girls The Role of Vitamin A  
Dr Martin Bloem
- 0845 A Comparison of Serum Retinol Levels with Hemoglobin Concentrations Before and After Vitamin A Capsule Distribution in One to Five Year Old Children in the Republic of the Marshall Islands  
Dr Neal Palafox
- 0855 Vitamin A and Beta-Carotene Status in Iodine Deficiency  
Dr Seyed Masoud Kimiagar
- 0905 Discussion
- 0925 Summary
- 0930 **The Bioavailability of Dietary Carotenoids**  
Dr James A Olson
- 0950 Discussion
- 1000 *Break and poster sessions with presenters available*  
**Micronutrient Interactions**  
**Experiences with Vitamin A Fortification of Foods**  
**Biologic Significance of Vitamin A Deficiency Infection**
- 1100 **Vitamin A Fortification of Foods**  
Co-Chairs Dr Guillermo Arroyave and Dr Juan R Aguilar
- 1100 Fortification Issues and Considerations  
Dr George Purvis
- 1120 Key Issues for Implementing a Program of Sugar Fortification with Vitamin A The Central American Experience  
Dr Guillermo Arroyave
- 1140 MSG Fortification in Indonesia Failure? Or Important Lessons?  
Dr Roy Tjong
- 1200 Discussion
- 1230 *Lunch*





• **Concurrent Sessions**

- 1430      **Experiences with Vitamin A Fortification of Foods**  
                  Chair Dr Max Blum  
                  Rapporteur Dr Venkatesh Mannar
- 1430      Sugar Fortification A Challenge of Vitamin A Deficiency in Honduras  
                  Dr Rosalinda Hernandez
- 1445      Retinol Stability of Fortified Sugar in Guatemala  
                  Dr Omar Dary
- 1500      Household Level Monitoring of Fortification Programs
- Ms Martha Burdick de Piedrasanta
- 1515      A School-distributed Cookie Is an Excellent Source of Vitamin A in  
                  Guatemala  
                  Ms Monica Guamuch
- 1530–1630      Discussion
- 1430      **Biologic Significance of Vitamin A Deficiency Infection**  
                  Chair Dr Richard Semba  
                  Rapporteur Dr Greg Hussey
- 1430      Vitamin A Status and Supplementation and Its Effect on Immunity in  
                  Children with AIDS  
                  Dr Greg D Hussey
- 1445      Effect of Vitamin A Supplements in Reducing Severity of Lower  
                  Respiratory Infection Among Children in Tanzania  
                  Dr M Guillermo Herrera
- 1500      Therapeutic Impact of Vitamin A Administration During Acute  
                  Diarrhea  
                  Dr Rajiv Bahl
- 1515–1615      Discussion
- 1630      End of day's formal sessions  
                  Set up for Wednesday's poster sessions  
                  Dietary Interventions  
                  Biologic Significance of Vitamin A Deficiency Growth and  
                  Inflammation  
                  Using Ethnographic Methods in Vitamin A Deficiency Research
- 1700–1900      **Interest Groups**  
                  Locations and topics to be announced

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Concurrent Sessions

- 0830            **Dietary Interventions**  
                  Co-Chairs Dr Vinodini Reddy and Dr Suttalak Smitasiri  
                  Rapporteur Dr Martin Bloem
- 0830            Crucial Elements in a Home Gardening Project—Experience from a  
                  Nationwide Program in Bangladesh  
                  Mr Aminuzzaman Talukder
- 0845            Does the Production of Dark Green Leafy Vegetables and Fruits Play a  
                  Role in the Etiology of Maternal Night Blindness, Diarrhea and  
                  Malnutrition in Bangladesh?  
                  Dr Martin Bloem
- 0900            Provitamin A Carotenoid Content of Common Foods  
                  Mr K Bhaskarachary
- 0915            Dietary Sources of Vitamin A Weighed Food Intakes of Preschool-Age  
                  Children in Rural Central Java, Indonesia  
                  Dr Michael Dibley
- 0930–1030    Discussion
- 0830            **Biologic Significance of Vitamin A Deficiency Growth and  
                  Inflammation**  
                  Chair Dr Paul Arthur  
                  Rapporteur Dr Kerth P West, Jr
- 0830            Reduction in Serum Retinol and Urinary Loss of Vitamin A in Children  
                  with Acute Diarrhea  
                  Dr Jose O Alvarez
- 0845            Epidemiology of Night Blindness During Pregnancy in Rural Nepal  
                  Ms Parul Christian
- 0900            Acute Respiratory Infections Prevent Improvement of Vitamin A Status  
                  in Young Infants Supplemented with Vitamin A  
                  Dr M M Rahman
- 0915–1015    Discussion
- 1030            *Break and poster sessions with presenters available*  
                  **Dietary Interventions**  
                  **Biologic Significance of Vitamin A Deficiency**  
                  **Growth and Inflammation**  
                  **Using Ethnographic Methods in Vitamin A Deficiency**  
                  **Research**
- 1130            *Lunch*



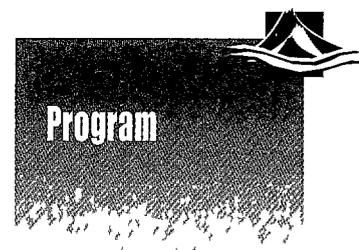


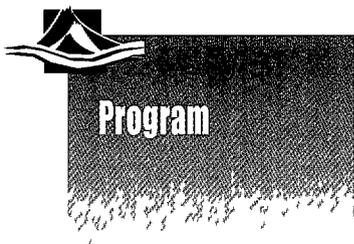
- 1330           **Summaries from Tuesday Concurrent Sessions**  
                   Chair Dr Hernan Delgado
- 1330           Experiences with Vitamin A Fortification of Foods  
                   Dr Max Blum
  - 1345           Discussion
  - 1400           Biologic Significance of Vitamin A Deficiency Infection  
                   Dr Richard Semba
  - 1420           Discussion
  - 1500           *Break*
  - 1530           **Using Ethnographic Methods in Vitamin A Deficiency Research**  
                   Chair Ms Elena Hurtado
  - 1530           Focused Ethnography for Community Assessment of Natural Food  
                   Sources of Vitamin A  
                   Dr Harriett Kuhnlein
  - 1550           Beliefs and Behavioral Factors Affecting Vitamin A Deficiency in Niger  
                   Ms Lauren Blum
  - 1610           Discussion
  - 1630           End of day's formal sessions  
                   Set up for Thursday's poster sessions  
                   Other Interventions for Prevention and Control of Vitamin A  
                   Deficiency  
                   Vitamin A Status Methodology
  - 1700–1830   **Interest Groups**  
                   Locations and topics to be announced
  - 1700–1900   **Video Presentations**  
                   Chair Ms Christa de Valverde
  - 1700           All We Expect Nutrition—A Basic Human Right  
                   Ms Jenny Cervinskaskas
  - 1730           Vitazucar  
                   Dr Juan Carlos Arraya and Ms Serena Rajabiun
  - 1735           Sugar Fortification in Guatemala  
                   ASAZGUA
  - 1750           Ammulla Dhon (Invaluable Treasure)  
                   Mr Sirajul Islam
  - 1805           Inauguration, Communication and Implementation of National  
                   Vitamin A Week  
                   Dr Sofia Begum and Dr Abdullah Al Momen
  - 2000–2130   **Interest Groups**  
                   Locations and topics to be announced

**Thursday, 21 March**

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- 0830      **Summaries from Wednesday Concurrent Sessions**  
            Chair Dr Donald McLaren
- 0830      Biologic Significance of Vitamin A Deficiency Growth and  
            Inflammation  
            Dr Paul Arthur
- 0845      Discussion
- 0900      Dietary Interventions  
            Dr Vinodini Reddy and Dr Suttalak Smitasiri
- 0950      Discussion
- 1030      *Break and poster sessions with presenters available*  
            **Other Interventions for Prevention and Control of  
            Vitamin A Deficiency**  
            **Vitamin A Status Methodology**
- 1130      **Developing Sustainable Solutions for the Problem of Vitamin A  
            Deficiency**  
            Chair Dr Ian Darnton-Hill  
            Rapporteur Dr Penelope Nestel  
            Introductory remarks Sustainability in Micronutrient Programs  
            Dr Martin Bloem
- 1145      Role of International Organizations  
            Dr Sonya Rabeneck
- 1200      South/South Technical Cooperation  
            Ms Catherine Siandwazi
- 1215      Role of the NGOs  
            Dr Miguel Artola  
            Ms Angela Churchill  
            Mr M Sirajul Islam
- 1230      Discussion
- 1300      *Lunch*





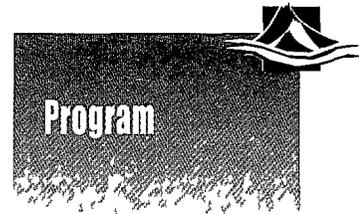
## Concurrent Sessions

- 1500 **Other Interventions for Prevention and Control of Vitamin A Deficiency**  
Chair Dr Moses Chirambo  
Rapporteur Mr David Alnwick
- 1500 Vitamin A Status of Zanzibari First-Graders Influence of Parasitic Infections and Impact of Deworming  
Dr James Tielsch
- 1515 Integration of Vitamin A Supplementation with EPI Programme in Bangladesh An Approach to Increase Coverage of Vitamin A Administration Among Infants  
Dr Mohammad Shahjahan
- 1530 Safety Aspects of Vitamin A Administration  
Dr Frank Chytil
- 1545 Use of Nutritional Surveillance Project (NSP) to Monitor Trends in Vitamin A Capsule Distribution  
Mr Abdul Hye
- 1600–1700 Discussion
- 1500 **Vitamin A Status Methodology**  
Chair Dr Clive West  
Rapporteur Dr Jean Humphrey
- 1500 Comparison of Hepatic Vitamin A Stores Estimated by the Deuterated Retinol Dilution Technique or by Analysis of Hepatic Biopsy Specimens in Bangladeshi Surgical Patients  
Ms Marjorie Haskell
- 1515 Vitamin A (HOLO-RBP) in Dried Whole Blood Spots by High Performance Capillary Electrophoresis (HPCE)  
Dr Jean Humphrey
- 1530 Modified Relative Dose Response (MRDR) Test for the Assessment of Vitamin A Nutritional Status in Children  
Dr N Raghuramulu
- 1545 Evaluation of Parameters of Vitamin A Status Using Data from Breastfeeding and Non-Breastfeeding Women  
Dr Saskia de Pee
- 1600 “Casual” vs “Full” Breastmilk Expression Effects on Measurements of Vitamin A  
Dr Chris Kjolhede
- 1615–1715 Discussion
- 1715 End of day’s formal sessions
- 2000 **Fiesta**

## Friday, 22 March

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- 0830      **Summaries from Thursday Concurrent Sessions**  
            Chair Dr Wilma Freire
- 0830      Other Interventions for Prevention and Control of Vitamin A Deficiency  
            Dr Moses Chirambo
- 0850      Discussion
- 0910      Vitamin A Status Methodology  
            Dr Clive West
- 0930      Discussion
- 1000      Break
- 1030      **Reports from Thematic Rapporteurs**  
            Chair Dr Abraham Horwitz
- 1030      Population Assessment  
            Dr Jean Humphrey
- 1050      Biologic Significance of Vitamin A Deficiency and Marginal Vitamin A  
            Deficiency  
            Dr Greg Hussey
- 1110      Appropriate Interventions  
            Ms Victoria Sheffield
- 1130      **Closing Remarks**  
            Dr Abraham Horwitz
- 1200      End of day's formal sessions



## Saturday and Sunday, 23–24 March

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Study tours organized by the local committee in Guatemala Preregistration required

**Sugar Fortification and Production of Fortified Foods**

0700, 23 March Departure

1800, 23 March Return

**Actions of Project Hope in the Western Highlands**

0700, 23 March Departure

1800, 24 March Return

**Vitamin A for Child Survival Program in Coban**

0700, 23 March Departure

1800, 24 March Return

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## Poster Sessions

### Monday / Poster Sessions

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#### Prevention and Control of Vitamin A Deficiency in Central America

- 1 Indirect Control for the Marketing of Fortified Foods—Sugar with Vitamin “A” and Salt with Iodine—Through Micronutrient Cantonal Schools  
Ms Nicté Ramirez
- 2 A Novel and Simple Quantitative Method to Determine Retinol in Fortified Sugar  
Ms Karla Andrea Molina
- 3 Identification of Cultivars of a Widely Consumed Mesoamerican Squash of High  $\beta$ -Carotene Content  
Dr Francisco Vasquez
- 4 By-products of the Refining of African Palm (*Elaeis guineensis*) Oil as a Source of Carotenoids and Fat  
Dr Alvaro Molina-Cruz
- 5 Validation of Messages About Vitamin A and Interventions in Groups at Risk  
Ms Yanira Elizabeth Ayala

#### Surveys

- 6 Vitamin A Deficiency in Three Micronesian Nations in the Pacific  
Dr Kennar Briand
- 7 National Vitamin A Survey in Lao PDR  
Dr Nicholas Cohen
- 8 Progress of Vitamin A Deficiency Control Program in Vietnam  
Dr Ha Huy Khoi
- 9 Xerophthalmia Prevalence in Ten Districts of the Far and Mid-Western Regions of Nepal  
Mr Bharat Ban
- 10 Green Leaves Are the Main Food Source of Vitamin A for Children in Some Areas of Niger  
Dr Helene Delisle
- 11 Assessment of Vitamin A Deficiency by Ophthalmological Examination, Serum Retinol Concentration and RDR Test in Preschool Zairean Children  
Dr Philippe Donnen
- 12 The Vitamin A Status of South African Children 6–71 Months of Age Results of the National Survey, 1994  
Dr Anna Coutsoudis and Dr Greg Hussey
- 13 Vitamin A Deficiency in Kenya  
Dr Duncan K Ngare
- 14 Vitamin A Deficiency and Children Food Consumption Between the Ages of 6 to 84 Months in Two Rural Areas of Guinea  
Dr Jean-François Schemann
- 15 Vitamin A Deficiency Prevalence Survey in Nicaragua  
Dr Gloria Elena Navas
- 16 Vitamin A Status in Three Age Groups of a Venezuelan Population  
Dr Liseti Solano Rodriguez
- 17 Prevalence and Risk Factors for Low Vitamin A in Peruvian Children  
Dr Luis Segura-Garcia
- 18 Vitamin A Status in Yaqui Indian School Children in Northwest Mexico  
Dr Mauro E Valencia J

## **Tuesday / Poster Sessions**

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### **Micronutrient Interactions**

- 1 Impact of Changes in Vitamin A Status on Response to Iron Supplementation in Infants  
Ms Christine Northrop-Clewes
- 2 Relationship Between Serum Vitamin A and Iron Status in Adolescent School Girls in Dhaka City  
Dr Faruk Ahmed

### **Experiences with Vitamin A Fortification of Foods**

- 3 Effect of Heat Treatment of Beta-Carotene Added to Soybean Cooking Oil in Rats and Humans  
Ms Rosa Maria Duarte Favaro
- 4 Fortification of Sugar with Vitamin A in Honduras Progress, Problems and Lessons Learned  
Dr Jose O Mora
- 5 Assessment of Vitamin A in Fortified Sugar—Simplified  
Dr Juan Carlos Arraya Tejada
- 6 Beta-Carotene Content in Fortified Brazilian Pasta and Evaluation of Analytical Methodology  
Dr Jaime Amaya-Farfan

### **Biologic Significance of Vitamin A Deficiency Infection**

- 7 Impact of Vitamin A Supplementation on Morbidity Pattern in Rural Preschool Children  
Dr Kailish Nath Agarwal
- 8 Vitamin A Supplementation in the First 6 Months of Life Does It Reduce Diarrhoea and ARI Morbidity?  
Dr Shams El Arifeen
- 9 Effect of Vitamin A Supplementation on the Incidence of Cough, Diarrhea, and Fever  
Dr M Guillermo Herrera



**Poster  
Sessions**

## Wednesday / Poster Sessions

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### Dietary Interventions

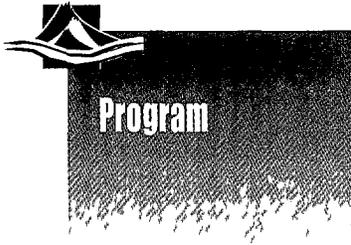
- 1 Prevention of Vitamin A Deficiency Through Horticultural Interventions  
Prof Indra Chakravarty
- 2 A Study on Different Interventions to Improve the Vitamin A Nutriture Among  
Preschool Children  
Dr Rajammal P Devadas
- 3 Promotion of Vitamin A-Rich Food Sources Through an Integrated IEC Program  
Ms Martha Burdick de Piedrasanta
- 4 Prevalence of Vitamin A Deficiency Among Adolescent Girls in Colombo, Sri  
Lanka and the Impact of Nutrition Education on Vitamin A Status  
Dr T M Sunethra Atukorala
- 5 A Simple Method to Evaluate Whether Consumption of Vitamin A-Rich Foods  
Increased and If So, Which Foods Results from Nutrition Intervention Activities in  
Two Regions of Niger  
Dr Susan Burger
- 6 Community Based Rehabilitation of the Malnourished Children Using Cereal-  
Vegetable Fortified Flours  
Ms Dolline Busolo
- 7 Indigenous Foods A Source of Vitamin A in Honduras  
Mrs Doris Chinchilla
- 8 Serum Retinol Levels in Preschool Children in Southern Ghana and the Effect of  
Cooking on the Beta-Carotene Levels of Commonly-Used Leafy Vegetables  
Dr Etor E K Takyi
- 9 ProVitA Household Distribution of Green, Yellow and Orange Plants as a Model  
System for Sustainable Provitamin A-Enrichment Projects Longitudinal Response  
of Biochemical Biomarkers  
Dr Jesus Bulux
- 10 Provitamin A Content of Vegetables Is Lower Than Reported in Food Tables  
Dr Saskia de Pee
- 11 Carotene-Rich Fruits and Vegetables Their Capacity to Improve Vitamin A Status  
of Children in West Java, a Comparison with Dietary Retinol Sources  
Dr Saskia de Pee

### Biologic Significance of Vitamin A Deficiency Growth and Inflammation

- 12 The Mechanism of Inflammation-Induced Hyporetinemia  
Dr Francisco J Rosales
- 13 Cord Blood Retinol and Retinol-Binding Protein in Healthy Preterm and Term  
Neonates and Neonates with Risk for Bronchopulmonary Dysplasia  
Ms Roxana Valdes-Ramos
- 14 Vitamin A and Intrauterine Growth Retardation  
Dr Patricia Rondo

### Using Ethnographic Methods in Vitamin A Deficiency Research

- 15 Looking for Long-Term Sustainability The Vitamin A Component of El Salvador's  
Nutrition Education Program  
Ms Irma Yolanda Nuñez
- 16 Why Children Don't Eat Their Vegetables An Anthropological Approach to  
Vitamin A Deficiency in West Java, Indonesia  
Ms Leslie Ellen Carlin



**Poster  
Sessions**

## Thursday / Poster Sessions

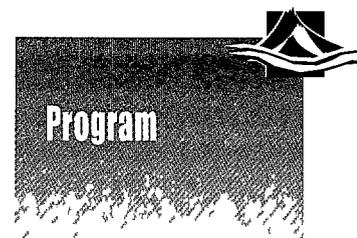
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### Other Interventions for Prevention and Control of Vitamin A Deficiency

- 1 Decreased Prevalence of Xerophthalmia and Improved Nutritional Status Among Preschoolers Following Vitamin A Supplementation and Nutrition Education Interventions in the Philippines  
Ms Ellen Villate
- 2 Contributing to Reduce the Nutritional Problem and Vitamin A Deficiency in Western Guatemala  
Dr Victor Calderon
- 3 Efficient Vitamin A Supply Through Inhalation  
Dr Hans K Biesalski
- 4 Effects of Vitamin A Supplements and Deworming with Albendazole on the Vitamin A Status of Indonesian Children as Assessed by a Simplified Modified Relative Dose Response (MRDR) Test  
Dr James A Olson
- 5 Prevention and Cure of Xerophthalmia Among Children in Southern India Are Improved by a Weekly Low-Dose Vitamin A Supplement  
Dr Roy C Milton

### Vitamin A Status Methodology

- 6 A Test of HKI Methods of Qualitative Assessment of Vitamin A Deficiency Problems in a Rural Area Near Pune, India  
Ms Viveka Persson
- 7 Evaluation of a Food Frequency Questionnaire to Estimate Vitamin A Intake in Preschool-Age Children in Indonesia  
Dr Michael J Dibley
- 8 Lutein as a Marker of Vegetable Intake and Vitamin A Status  
Dr David I Thurnham
- 9 A Modified Method to Minimise Losses of Carotenoids and Tocopherols During HPLC Analysis  
Mr Georg Lietz
- 10 Linking a Vitamin A Deficiency Risk Assessment Questionnaire with a Serum Retinol Vitamin A Deficiency Prevalence Study in the Republic of the Marshall Islands  
Dr Kennar Briand
- 11 Differences in Serum Retinol Concentrations in Mother-Infant Pairs at Birth by Ethnic Origin in the Negev (Southern Israel)  
Dr Rafael Gorodischer
- 12 Prevalence of Subclinical Vitamin A Deficiency Among Young Infants in Bangladesh  
Mr M A Wahed



**Poster  
Sessions**

⋮



## **IVACG Steering Committee**

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Moses C Chirambo, MD  
Frances R Davidson, PhD,  
IVACG Secretary  
Abraham Horwitz, MD, MPH,  
IVACG Chair  
Vinodini Reddy, MD, DCH, FIAP  
Leonor Maria P Santos, PhD  
Suttalak Smitasiri, PhD  
Alfred Sommer, MD, MHSc,  
IVACG Steering Committee Chair  
Barbara A Underwood, PhD  
Keith P West, Jr, DrPH

## **Local Organizing Committee in Guatemala**

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Dr Hernan L Delgado, Coordinator  
Instituto de Nutricion de Centro  
America y Panama  
Ministerio de Salud Publica y Asistencia  
Social  
Asociacion de Azucareros de Guatemala  
CeSSIAM  
Comite Prociegos y Sordos de Guatemala  
Fundacion Internacional del Ojo  
Oficina Panamericana de la Salud  
Proyecto HOPE  
Proyecto Salud Materno-Infantil  
Comunidad Economica Europea  
Programa Mundial de Alimentos  
UNICEF  
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## **IVACG Secretariat Staff**

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Laurie Lindsay Aomari, RD  
Diane Dalisera, MBA  
Maribel Flewitt  
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Dwayne Milbrand

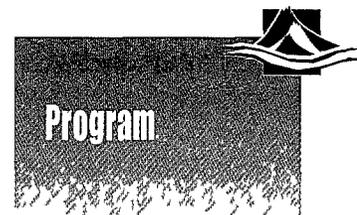
## **Contributors to the XVII IVACG Meeting**

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The XVII IVACG Meeting is sponsored by the Local Organizing Committee coordinated by Instituto de Nutricion de Centro America y Panama, and IVACG. Much of the meeting was organized with funding from Opportunities for Micronutrient Interventions (OMNI), a project of the Office of Health and Nutrition, Global Bureau for Programs, Field Support and Research, U S Agency for International Development.

The IVACG Secretariat gratefully acknowledges the additional contributions of the following individuals and organizations:

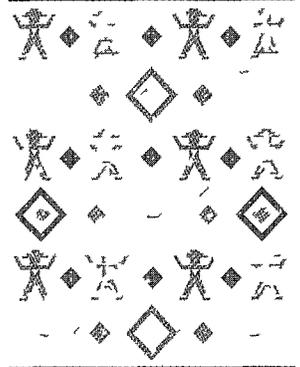
ANACAFE—Departamento de  
Accion Social  
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BASF de Guatemala, S A  
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Productos ROCHE, S A  
Task Force SIGHT AND LIFE  
Universidad Del Valle



## **Contributors**



# Summary



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**T**he XVII International Vitamin A Consultative Group (IVACG) Meeting was inaugurated amid the beautiful background of Guatemala City, the capital of Guatemala, a country that is considered the heart of Mayan civilization. A total of 488 participants from 65 countries attended the meeting.

Dr Abraham Horwitz (1) welcomed the meeting participants and noted the need to focus on the meeting's importance in contributing to new knowledge and creating a strengthened collaboration to eliminate vitamin A deficiency (VAD). He also referred to Mr Philip Musgrove of the World Bank, who described the serious consequences of VAD and showed that the prevention and control of it are highly cost effective. This is why priority should be given to this health and nutrition problem where it exists. Dr Horwitz called for governments to reinforce surveillance of VAD and communicate with international organizations to analyze their progress. He also stressed the need for all concerned to focus on solutions to eliminate VAD. To bring about the virtual elimination of VAD will entail understanding different approaches in different countries.

Dr Hernan L Delgado, director of the Institute of Nutrition of Central America and Panama (INCAP) and coordinator of the local committee (2), welcomed the participants and expressed wishes for a successful meeting. He also noted the willingness of Guatemala to share its experiences and the progress it has made in combating VAD. Dr Delgado reviewed the objectives for this meeting:

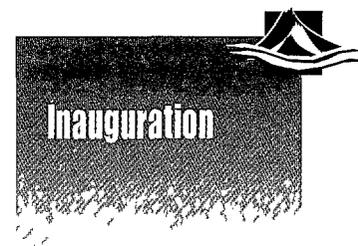
- ◆ Provide a forum for exchanging ideas and new information to improve and strengthen interventions aimed at reducing childhood mortality and morbidity by improving children's vitamin A status
- ◆ Translate the latest research findings on vitamin A to improve intervention strategies

- ◆ Share practical experiences in planning and promoting sustainable programs for improving a population's vitamin A status
- ◆ Strengthen linkages between the public and private sectors, nationally and internationally, to maximize resources available for vitamin A programs
- ◆ Identify knowledge gaps and operational barriers that constrain the effectiveness of efforts to prevent and control VAD from the community to the national level

During the inauguration, there was a presentation of awards to honor Dr Guillermo Arroyave and Dr Elisa Molina de Stahl for their contributions to the successful implementation program for fortifying sugar with vitamin A in Central America.

Dr George A O Alleyne (3), director of the Pan American Health Organization, recognized Guatemala as an appropriate host for IVACG. He also recognized INCAP for its achievements and contributions to alleviate VAD and called for partnership among organizations to work together toward the same goals. He closed his remarks by congratulating IVACG for its work.

Guatemala's Minister of Public Health and Social Welfare, Ing Marco Tulio Sosa Ramirez (4), noted that, on behalf of the government and the president, Guatemala was proud to host the IVACG meeting. He noted that Guatemala has pioneered efforts to fight VAD, which causes serious eye lesions and adverse health problems. Guatemala concentrates its efforts to eliminate VAD on a collaboration between the government and the sugar industry to fortify sugar with vitamin A, which has resulted in a marked decline of severe VAD in Guatemala. He then expressed his gratitude for the knowledge that would be contributed at this meeting and declared the meeting open.





**D**r Jesus Bulux (5) presented a panorama of the situation in Central America. Although it is a small area, the region has vast geographic, economic, and cultural diversity as well as a diversity of ethnic groups and languages.

In 1966 INCAP undertook the first survey of the magnitude of VAD, which has been an important catalyst in developing strategies and plans of action to combat VAD in Central America. The task has not been easy because of the considerable diversity of the region. Representatives of each of the seven Central American countries then described work done in their nations to prevent and control VAD.

Dr Jose Antonio Lopez, Director General of Health Services, Ministry of Health, Belize (6), presented an overview of plans of action for his country. No national survey to assess the vitamin A status of the population has been conducted, although a survey of consumption of vitamin A-rich foods showed that Mayan groups had lower consumption than Mestizos and Asians. Belize has limited sources of vitamin A-rich foods, and attempts are being made to promote increased consumption of these foods, especially in vulnerable groups. No fortification of foods is taking place, although fortification of sugar with vitamin A is being considered. To reduce costs and to share expertise, consideration has been given to the possibility of negotiating with other countries that are currently fortifying sugar.

Dr Rosa Maria Novygrodt, director of the Nutrition Department, Ministry of Health, Costa Rica (7), described the situation in her country. The 1966 INCAP survey revealed that 32% of preschoolers had low serum retinol levels. In 1974, sugar was fortified with vitamin A and this practice continued until 1980, when studies revealed improvements in vitamin A consumption and in the prevalence of low serum retinol levels.

The improvement was not attributed solely to the sugar fortification program, as other primary health care programs were also operating at this time. A national survey is planned for 1996 to provide information on the current nutritional status of the population.

Dr Eduardo Interiano, Minister of Health, El Salvador (8), presented information from his country. The 1966 INCAP survey showed a 31% prevalence of low serum retinol levels, in the 1988 survey, there were still high prevalences of low serum retinol, with the largest problem in rural areas where 40% of the population had low serum retinol levels. From 1990 some of the sugar was fortified but the Vitamin A Sugar Fortification Law was not created until 1994. In the 1994-1995 harvest, 74% of the sugar for household consumption was fortified, the goal is to reach 100% fortification for this year's harvest. Quality control systems are being implemented for monitoring vitamin A level in sugar at the mills, markets, supermarkets, and stores. The success of the sugar fortification program has been attributed to the partnership between the ministry of health and the private sector. Other activities include supplementation of preschoolers with 200,000 international units (IU) of vitamin A capsules and nutrition education regarding vitamin A in school programs. As part of the community health program, children less than 5 years old receive 50,000-IU vitamin A capsules.

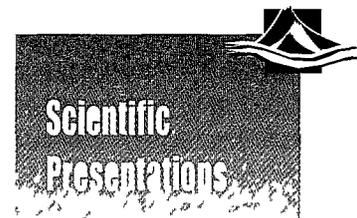
Dr Carlos Andrade, Vice Minister of Public Health and Social Welfare, Guatemala (9), presented an overview of Guatemala's action plans. The 1966 INCAP survey revealed that 26.2% of children under 5 years old had low serum retinol levels. In 1974, Guatemala became a pioneer in the struggle against micronutrient deficiencies in Latin America, especially in the field of food fortification. Fortification of sugar with vitamin A became mandatory and its introduc-

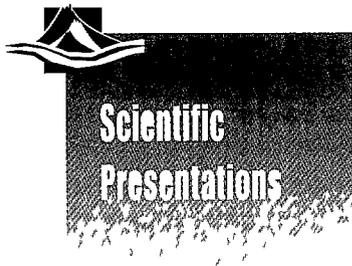
tion resulted in a substantial reduction in VAD. Difficulty in sustaining the program led to its suspension in 1982. The program was reinitiated in 1988, and in 1995 a nutritional survey was conducted to update existing information. The results revealed that moderate VAD is found among children 1–5 years old (15.8%), the highest percentage of deficiency is found among children who consume “panela” (molasses or raw sugar) instead of fortified sugar (22.4%). Law enforcement and involvement of sugar producers in drawing up the regulations were seen as important factors for sustaining the project. Although there has been considerable progress in fortifying sugar, one of the limitations is governmental control and monitoring of the program. Other interventions include distribution of iron- and vitamin A–fortified cookies in the schools, vitamin A supplementation to women of childbearing age and to children under 5 in high-risk regions, development of infant foods fortified with vitamin A, and nongovernmental organization (NGO) programs such as integrated strategies used in child survival programs.

Dr Virginia Espinoza, Vice-Minister of Health, Honduras (10), presented her country’s action plans. The 1966 INCAP survey revealed that 22% of the population had low serum retinol levels. In 1976, a vitamin A fortification law was approved and partial implementation took place at intervals until 1988, when fortification was again instituted as a result of the 1987 nutritional survey. This survey showed that VAD had not decreased, 18% of children under 5 and 39% of women still had low serum retinol levels. This year the goal is to reach 100% fortification of sugar with vitamin A, although there are still problems with quality control and distribution from the sugar mills to the home. In 1992 the Ministry of Health developed a micronutrient deficiency strategy for prevention and control of micronutrient deficiencies, which involves fortification

of sugar with vitamin A, targeted vitamin A capsule distribution, and training activities, education, and communication for information dissemination and promotion of family production, food conservation, and consumption of foods rich in vitamin A. Special emphasis was placed on training personnel of the Ministry of Health and Ministry of Education as well as incorporating micronutrient information into the medical and nursing curricula. In addition, print and audiovisual educational materials were designed, pretested, produced, and distributed to support activities for prevention of VAD. As with El Salvador and Guatemala, the success of sugar fortification in Honduras has been attributed to partnership and consensus building between the Ministry of Health and the sugar industry.

Dr Federico Muñoz, Minister of Health, Nicaragua (11), presented the information for his country. The 1966 INCAP survey revealed a prevalence of 26% of children with low serum retinol levels. Then Nicaragua suffered from earthquake, war, and hurricanes, with constant declines in income and nutritional status. To assess the current vitamin A situation and to plan appropriate control programs, a national survey of vitamin A status of children under 6 years old was conducted in 1993 and showed clearly a decline in the vitamin A status, with 31% of children having low serum retinol levels. In addition, the survey showed that 70% of the children consumed less than 70% of the daily recommended intake of vitamin A. Consequently, the government of Nicaragua has begun an emergency vitamin A supplementation program aimed at young children. In 1994–1995, 69% of children under 5 years old were reached. Additional programs include the use of micronutrient-fortified biscuits and milk fortified with vitamins A and D. The feasibility of fortifying sugar with vitamin A is being discussed among sugar cane producers and the Nicaraguan government.





Dr Jorge Montalvan, Director General of Health, Panama (12), also presented information. The 1966 survey showed that 18% of children in Panama under 5 years old had low serum retinol levels and dietary intake surveys showed that 25% of families consumed less than 15% of the recommended dietary allowance for vitamin A. In 1976, legislation was passed to allow fortification of sugar with vitamin A, but the program was not implemented. Panama's current Plan of Action for 1993–1997 aims at providing high-risk groups with megadoses of vitamin A at both the community level and the clinic level. Coordination with the maternal and child health program

has been successful in ensuring that the "Road to Health" card now has a space allocated for registering vitamin A doses. In addition, they plan to use a variety of media, e.g., magazines, radio, and television, to implement an education program. The magazine *Vitamin A Source of Health and Child Survival* has been successfully distributed. Health teams at the regional and national level are being trained in prevention of VAD.

The session on Central America's experiences also included five poster presentations, which highlighted some of the advances in vitamin A research in the region (13–17).

## **VIRTUAL ELIMINATION OF VAD OBSTACLES AND SOLUTIONS FOR THE YEAR 2000**

### **PRESENTATION OF THE MEETING THEME**

Dr Abraham Horwitz (18) stated that the goal agreed upon at the World Summit for Children and at the International Conference on Nutrition is virtual elimination of VAD by the year 2000. This goal should be included in national nutrition policies and/or the country nutrition plans of action. However, there are obstacles to overcome and solutions that must be designed and implemented before the goal can be reached. These are the basis for the theme of this meeting, "Virtual Elimination of Vitamin A Deficiency: Obstacles and Solutions for the Year 2000." Obstacles can be political, economic, and cultural. Where a vitamin A program is linked to health and other sectoral infrastructures, poor coverage of services can become an obstacle. From the food aspects, the availability of vitamin A food sources as well as a lack of knowledge about the content and bioavailability of carotene-rich foods should be considered. Food fortification is a multifaceted process that requires integration of several factors ranging from selecting a food staple, determining appropriate technology, pricing the fortified food, and creating awareness on

one end to legislation, regulation, enforcement, monitoring, and evaluating impact of programs on the other. From the program point of view, lack of effective management and absence of coordination among different sectors of development represent frequently encountered obstacles. Some solutions to overcome these barriers are to periodically analyze the magnitude and characteristics of VAD, inform decision makers about the significance and application of scientific data, strengthen information, education, and communication to change the behavior of people toward prevention of VAD, and, quite importantly, effectively manage VAD prevention and control programs.

### **PRESENT STATUS AND GLOBAL PROGRESS TOWARD THE YEAR 2000 GOAL**

Dr Barbara Underwood (19) reminded the participants of the challenge ahead, the 10-year goal based on the 1990 World Summit for Children, which aims to "virtually eliminate vitamin A deficiency and *all* its consequences including blindness." The mid-decade goal of "ensuring at least 80% of children under

24 months of age receive adequate vitamin A through a combination of strategies" passed at the end of 1995. Although progress was made, the goal was not met on a global basis. Only 1750 days remain until the end of the year 2000 and the question is whether the 10-year goal can still be met.

The first global mapping of VAD occurred around the mid-1970s. The world was divided into three regions based on the frequency of xerophthalmia: developed countries with no xerophthalmia, rice-growing countries in Asia where xerophthalmia is a public problem, and the rest of the world where the problem is intermittently intensive. In the early 1980s, a community survey in Indonesia led to an extrapolation for Asia of 200,000–400,000 cases of corneal and 4–8 million cases of noncorneal xerophthalmia annually. A later projection, based on conjunctival impression cytology data, indicated that 40–80 million children worldwide suffer from subclinical VAD.

The global problem of VAD was mapped in 1984 in the report of a Joint World Health Organization (WHO)/United Nations Children's Fund (UNICEF)/United States Agency for International Development (USAID)/Helen Keller International (HKI)/IVACG meeting where, based mainly on the prevalence of xerophthalmia, countries were divided into categories A and B (public health problem of VAD), C (VAD is likely to be a problem), and D (no problem or no data available). This map generated a lot of controversy as well as activity. Three years later, WHO revised the map. 22 countries were classified as having a significant public health problem in part or all of the country, 15 had insufficient information but a high probability of a significant VAD problem, and 25 countries had sporadic cases of VAD, not sufficient to constitute a public health problem. In preparation for the International Conference on Nutrition in 1992, WHO estimated global figures of nearly 14 million children with xeroph-

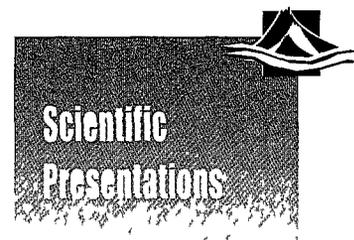
thalmia and 190 million at risk of sub-clinical deficiency.

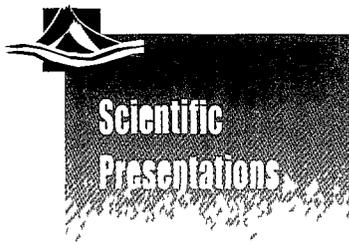
On the basis of expert consultation, WHO has redefined the public health magnitude of VAD to include the sub-clinical stage and has categorized the severity of the problem according to serum values of less than or equal to 0.70  $\mu\text{mol/L}$ . This new definition resulted in a map of clinical and subclinical VAD that was presented at the XVI IVACG Meeting in 1994. The clinical problem has markedly declined from 14 million in 1994 to 3 million, whereas subclinical deficiency has increased from 190 to 230 million children. Surveys have been conducted in 29 countries to update the information. The 1996 map revealed that 22% of WHO Member States have a clinically significant problem and nearly 25% of them have subclinical problems of varying severity. Data are lacking in approximately one-third of WHO Member States and the remainder (about 20%) have no problem. On a regional basis, Southeast Asia and Africa account for just under 90% of the global problem. Clinical VAD occurs primarily in Asia, Africa, and Western Pacific regions. During the past 10 years, substantial progress has been made, particularly in establishing national programs in most countries as well as in generating data about the vitamin A situation. Countries are urged to accelerate their efforts to meet the 10-year goal of virtually eliminating VAD.

## COUNTRY EXPERIENCES

### *India*

Dr Vinodini Reddy (20) indicated that VAD has been recognized as a major public health problem in India. Large-scale intervention programs, including supplementation, fortification, and dietary diversification, have been launched to reduce the prevalence of deficiency. Although recent surveys show a declining trend in the prevalence of xerophthalmia, virtual elimination of





VAD by the year 2000 remains a challenge

Analysis of nutrition programs in India shows five distinct phases. Clinical studies conducted during the 1960s led to understanding the causes and consequences of xerophthalmia, development of simple methods for diagnosis and treatment, and, eventually, better management of cases. But soon it was realized that an individual approach to case management will not solve the problem in the community.

Periodic administration of large doses of vitamin A was suggested as a way to tackle the problem at the community level. Extensive field trials carried out by the National Institute of Nutrition in Hyderabad demonstrated the feasibility and efficacy of this approach.

A national vitamin A program launched in 1972 provided a single dose of 200,000 IU of vitamin A every 6 months to all children 1–5 years old. Evaluation of the program revealed poor coverage because of inadequate supplies, poor coordination between various health functionaries, and lack of supervision. Efforts were made to overcome the problems. It has become apparent that the problem of VAD cannot be solved in isolation. In the revised strategy, delivery of vitamin A is linked with the immunization program and is implemented as part of the Integrated Child Development Service program. The vitamin A supplementation program has been in operation for more than 2 decades, even though it was planned as a short-term measure. Because the root cause of VAD is inadequacy of dietary intake, emphasis has shifted to long-term food-based interventions, particularly production and consumption of carotene-rich foods through horticulture and education programs.

A National Plan of Action for Nutrition has been formulated recently. It is recognized that malnutrition results from socioeconomic deprivation, and measures outside the scope of the health sector are necessary to overcome the

problem. Emphasis is therefore placed on a comprehensive multisectoral strategy involving various sectors including health, agriculture, food, education, women, and child development to implement programs, including specific measures to combat VAD. The challenge lies in establishing mechanisms of coordination for converging services at the community level.

### **Indonesia**

The experiences of Indonesia were presented by Dr. Martin Bloem for Dr. Fasih Jalal (21). VAD was recognized as a problem during the Dutch-governed period of the mid-1940s, but no specific program was implemented. Later, in the early 1960s, an integrated concept of planning, research and development, and program implementation was introduced. The planning part is under the Ministry of Planning, and nutrition is recognized as one of the essential components for human resource development, the research and development aspect is the mission of the Nutrition Research and Development Center, and the Directorate of Community Nutrition under the Ministry of Health is responsible for implementing nutrition programs. It was noticed that the most severe sign of VAD, xerophthalmia, stemmed from a multifactorial etiology and often was associated with the poorest group of the society.

In 1976, VAD was reported to be a significant problem in Indonesia. Since then, multistrategy programs to combat VAD have been launched: a medical program that provides vitamin A supplements (200,000 IU) twice a year to preschool children via the local health post or *posyandu*, fortification of monosodium glutamate (MSG) with vitamin A, and the food availability program, which deals with the agricultural approach. Studies carried out in Indonesia in the early 1980s showed that subclinical VAD can adversely affect health to the degree that it carries public health consequences. A 1992 survey indicated

that Indonesia was xerophthalmia-free, but subclinical VAD still existed at a disturbing level, and there were pockets of severe VAD among the very poor

At present, the medical approach covers only those in poverty, whereas fortification uses multiple vehicles and reaches the broader population. The government plays a supervisory role in the current fortification strategy and does not take the initiative as it did with MSG. The poverty reduction program was carried out along with food diversification as well as the school feeding programs, whereas the Ministry of Planning is responsible for the agricultural approach. The promising feature is that Indonesia is launching the poverty reduction program when the country is economically ready for it, thus ensuring a satisfactory level of outcome. Poverty alleviation also makes possible cost-effective implementation of the medical approach to VAD.

### *Ghana*

Dr Rosanna Agble (22) presented the case of the national VAD control program in Ghana. The reasons for setting up a national program are as follows:

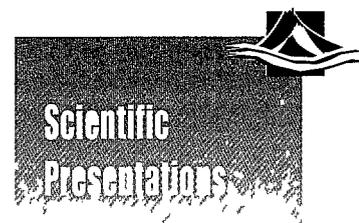
1. The magnitude of the problem is apparent in the northern part of the country, but isolated studies recently indicated a problem in the south as well.
2. The Ghana Vitamin A Supplementation Trials (VAST) demonstrated the efficacy of supplementation.
3. Recent initiatives in the use of vitamin A in the treatment of measles need to be coordinated in a national program.

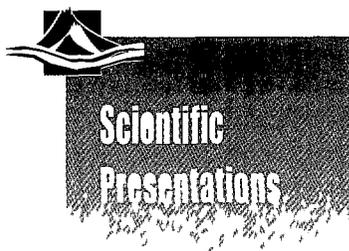
There are four components of the national program: a) policy on vitamin A for treatment of measles, b) supplementation with different strategies used in the North, such as the Expanded Programme on Immunization (EPI) and other health contacts, and child-to-child and community-based distribution, c) describing the situation in the southern part of the

country, and d) exploring potential dietary interventions. Much progress has been made: the formal policy position to tackle VAD has been adopted by the Ministry of Health, funding has been made available, consensus has been reached between the national and regional implementors and policy makers, a multisectoral coordinating group has been formed, and the regional teams are readying their plans for implementation. The major obstacles have been identified as inadequate advocacy both internationally and locally, central control and bureaucracy within the Ministry of Health, a variable picture of the VAD problem, which will involve different strategies in various parts of the country and different sectors, and the lack of an easily seen indicator (unlike goiter). The following solutions were suggested: improve political advocacy (this is already being addressed), adopt more flexible time frames for program implementation from donors, make a commitment to follow-up policy and program development after research (this needs to be built into research proposals), and obtain commitments from government at the stage where research proposals are being negotiated.

### *Tanzania*

Tanzania's experience in combating VAD was presented by Dr Godwin Ndossi (23). Tanzania has no national data on the problem, however, various surveys and hospital-based xerophthalmia records indicate that VAD is a problem of public health significance in different parts of the country. The Tanzania Food and Nutrition Centre estimated that VAD affects about 1.4 million people or 6.1% of the population, the majority of whom are children under 6 years old. In 1985, the first 5-year national program (1985–1990) for prevention and control of VAD was launched. The major interventions were supplementation and dietary/horticultural approaches combined with public health measures within maternal and child health, the immunization





program, and the Child Survival and Development program. Capsules containing 50,000 IU of vitamin A were administered to high-risk children (6 months to 6 years old) who were malnourished or who had measles, diarrhea, or clinical signs of VAD. The capsules were distributed through the Essential Drug Program. Dietary approaches have focused mainly on promotion of production and consumption of foods rich in vitamin A, fats, and protein and promotion of breastfeeding and appropriate weaning foods. Fortification of foods with vitamin A has been limited to locally produced margarine, imported baby formula, and weaning foods, however, these foods reach an insignificant proportion of the target population. The national program supportive activities include research and development, information, education, and communication (IEC), laboratory and information management, and program logistics and coordination. The program strategies were multisectoral and multidisciplinary in nature.

The major achievements between 1985 and 1990 include reactivation of the National Prevention of Blindness Committee, formulation and implementation of the Tanzania Prevention of Blindness Program as well as the first 5-year National Vitamin A Program, and formation of a National Vitamin A Consultative Group to act as a policy and steering body for National Program implementation. As evidence of program effectiveness, prevalence of low serum retinol ( $<10 \mu\text{g/dL}$ ) decreased from 17.6% of the population in 1988 to 1.3% in 1990 in the Shingyanga region. The constraints of the first 5-year program were inadequate technical expertise, lack of awareness of the problem among policy makers and communities, and lack of problem assessment and analysis tools.

The second 5-year program, covering 1990–1995, was launched with the emphasis placed on IEC and social marketing as well as community partici-

pation. The increased awareness among policy makers at various levels made the program implementation much smoother, and more collaboration was fostered among governmental and nongovernmental organizations. The major achievements during this period include incorporation of nutrition into training curricula of various institutions, a pilot project on production of vitamin A-rich fruits and vegetables, research to improve traditional solar drying technology, and nationwide training for health professionals for diagnosis and management of clinical VAD. Despite these achievements, there are constraints, such as unavailability of financial and adequate human resources, poor communication infrastructure, and the need to strengthen management at the regional and community levels.

## COUNTRY SURVEYS

Table 1 summarizes the results of surveys in several countries (24–36) for prevalence of VAD, which were presented at the XVII IVACG Meeting.

## RESPONSE PANEL

The response panel, composed of Dra Maria del Carmen de Daroca from Bolivia, Mr. Ram K. Shrestha from Nepal, Prof. Ha Huy Khoi from Vietnam, and Dr. Paul Arthur from Ghana, raised the following issues:

*What is the best way to work with policy makers, especially in a country free of xerophthalmia?*

Panelists said that the International Conference on Nutrition should support existing health programs that advocate inclusion of micronutrients. Allotment to sustain such programs must be budgeted early in the planning stage. In addition, communication with policy makers must include both clinical and subclinical aspects of the problem. NGOs and international agencies can also publicize the serious nature of subclinical VAD.

**TABLE 1 SUMMARY OF REPORTED VITAMIN A STATUS AND DIETARY INTAKE SURVEYS**

REGION/country (reference)	N	Age (months)	Serum retinol		RDR/MRDR	CIC	Xerophthalmia			Vitamin A intake
			$\mu\text{mol/L}$ <0.70	$\mu\text{mol/L}$ <0.35	Abnormal	CIC	XN	X1B	X2/X3	<70% RDA
			%	%	%	%	%	%	%	%
<b>ASIA</b>										
Lao PDR (25)	3376	0-71								
	680	Adult						0.7		
		women						0.2		
		Pregnant						0.9		
		Lactating						0.5		
Nepal (27)	18920	6-60						1.4	3.1	0.2
Vietnam (26)	34214	0-60						0.4	0.2	0.1
<b>PACIFIC (24)</b>										
Kiribati	4614	6-60							14.7	
Chuuk State		36-72				50				
	218	18-34	55.0	11.0						
	157	36-72	76.0	20.0						
Marshall Islands	444	12-60	63.0	8.0						
<b>AFRICA</b>										
Guinea (32)	1500	6-84								
Mountain								0.6	0.1	
Plain								0.0	0.05	
Kenya (>1)	6425	6-72	40.6	7.7					1.0	0.1
Niger (28)	471	24-48								
Bouza (B) and	144					74 (B)				47 (B)
Ouallam (O)						77 (O)				6 (O)
District										
South Africa (30)	11430	6-71	33.0	3.0				12	0.4-0.8	0.2-0.7
Zaire (29)	415	6-60		19.7	7.6			0.7		
<b>SOUTH AMERICA</b>										
Mexico (36)	300	72-120	46.3	6.3						
Nicaragua (33)	1791	12-60	29.0							70.0
Peru (35)										
Lima	225	0-48	5-24							
Coast	94	0-48	21.0							
Highlands	74	0-48	24.0							
Venezuela (34)	75	0-72	16.5	0.0						61.0
	425	73-144	10.6	2.1						66.6
	99	>65 Years	8.1	4.0						80.8

RDR = relative dose response MRDR = modified relative dose response CIC = conjunctival impression cytology XN = night blindness  
X1B = Bitot's spot X2/X3 = keratomalacia RDA = recommended dietary allowance

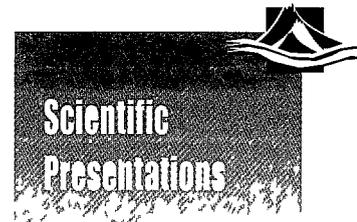
*How can the lack of coordination among different sectors be solved?*

Suggestions were made to form a national committee or national advisory board consisting of representatives of different ministries. The national research center can serve as a technical consultant to these committees. It is important to obtain consensus from as many different sectors as possible before launching a program.

*Investment in local versus international research with constraint of resources*

The response was supportive of investing in operational research that is coupled with local program implementation needs, is applicable to more than one program, and can be applied in other settings.

*What can be suggested to address future problems with a national vitamin A capsule supplementation program?*





The suggestion was to create a solid national mechanism and for the program to be as self-reliant as possible

*Incorporation of short-term supplementation into a long-term approach*

No single strategy will solve the problem, so planners should not isolate different strategies into the short, medium, and long term but rather should begin with multiple strategies along with relevant supportive activities

**RESPONSE OF USAID**

Dr Nils Daulaire (37) presented the response of USAID to the global challenge of VAD. As one of the most important funding agencies for vitamin A programs, USAID has made a long-term commitment and believes this investment has paid off. Twenty-two years ago, USAID initiated and supported IVACG. Over these 2 decades, we have learned that VAD affects child health and survival and that vitamin A is the single most cost-effective tool to reduce child mortality in deficient populations. Vitamin A interventions support USAID's fundamental mission of sustainable development.

Strategies to combat VAD can be integrated into routine services such as programs to eradicate poverty and food insecurity. Another opportunity is the global goal to eradicate polio by the year 2000. To reach this goal, there are periodic intensive efforts to reach every child,

therefore, addition of the vitamin A strategy to the EPI program should be helpful. Dr Daulaire encouraged inclusion of vitamin A supplementation on national immunization days and suggested using vitamin A as a spearhead for primary health care.

Dietary solutions to VAD are also being sought, and this is a slow process. Dr Daulaire said that meeting participants can envision the day when fortification and supplementation may be needed only in certain situations. He cautioned that *that day* should not be confused with *today*.

Emphasis should be placed on research and technology development as well as the working relationship between the public and private sector—just like marrying the “what” with the “how” Partnership, not competition, of different strategies to combat VAD should be encouraged.

On behalf of USAID, Dr Daulaire reiterated the agency's support to achieve the goal of eliminating VAD by the year 2000. It is now agency policy that VAD should be addressed wherever USAID supports programs to reduce child mortality, and the agency will stress the need for results. Despite budget constraints, USAID will try to allot a considerable amount to the child survival and micronutrient deficiency programs. USAID will seek this opportunity to continue working together with other agencies and all parties concerned with the virtual elimination of VAD.

**MICRONUTRIENT FORUM**

This session, chaired by Dr Frances Davidson, highlighted the growing awareness of the need to consider iron and iodine deficiencies in conjunction with VAD.

**VITAMIN A AND IRON INTERACTIONS**

The interactions between iron and

vitamin A were considered in two oral presentations (38, 39) and in two posters (40, 41).

Palafox et al (38) conducted their study in the Marshall Islands in 800 children 1–5 years old, and they found a 60% prevalence of VAD and a 36% prevalence of anemia. He reported a high correlation between retinol and hemoglobin. The children were supplemented

with 200,000 IU of vitamin A, and 1 month later blood was drawn from a random sample of the original 800 children studied. Only 26 of the original 800 children had blood taken both pre- and postsupplementation. In these 26 children, there was a significant increase in serum retinol levels and a slight increase in hemoglobin, ferritin, and serum iron, however, the sample size was insufficient to make conclusive statements about the significance of these findings.

Northrop-Clewes et al (40), in a randomized double-blind trial, supplemented 300 infants with 15 mg of iron or placebo daily for 12 weeks. The period of supplementation coincided with the summer season, when there is an increased intake of fruits and vegetables, and the authors found an increase in serum retinol in the group as a whole. Hemoglobin levels increased in the supplemented group, however, the authors noted that those children who were in the supplemented group and who also had low vitamin A status probably had more new infections as interpreted by increased  $\alpha$ 1-antichymotrypsin and ferritin. Both are acute-phase reactants that increase in infection. This effect was not seen in those iron-supplemented children who had adequate vitamin A status. From their data, the authors made the important point that administering iron supplements to infected children may exacerbate inflammatory damage in infections. Ensuring that children have adequate vitamin A status when iron supplements are administered may be important to counter the potentially toxic effects of iron supplements.

Martin Bloem reported results from a study conducted by Angeles et al (39). In this placebo-controlled study, 281 Indonesian adolescent school girls (middle-income group) received vitamin A and

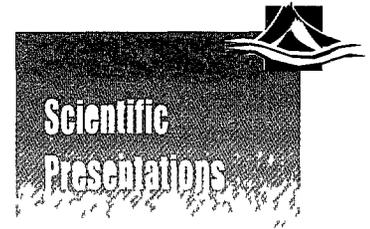
iron supplements in one of three different regimens. The authors showed that delivering iron supplements once per week as opposed to daily dosing was as effective in increasing hemoglobin, and that a lower dose of 60 as opposed to 120 mg per week was more effective in increasing hemoglobin levels. They found that combining 20,000 IU of vitamin A together with the 60 mg iron dose was most effective in increasing hemoglobin levels.

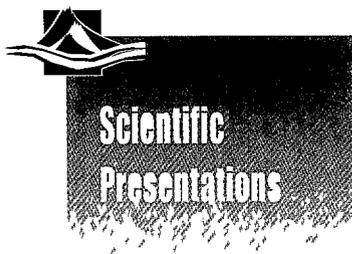
Ahmed et al (41) also investigated the interaction between vitamin A and iron in adolescent girls. In their study conducted in Bangladesh, they found significant positive correlations between serum vitamin A and hemoglobin, packed cell volume (PCV), and serum iron. They confirmed the issue raised by others that an inadequate vitamin A status may compromise the effectiveness of iron supplementation in such situations.

In the interest group discussion held to further consider micronutrient interactions, the group decided that, although the evidence suggests an association between iron and vitamin A, iron cannot be used to correct VAD and that an adequate vitamin A status in an individual is important before iron supplements are administered.

## VITAMIN A AND IODINE INTERACTIONS

Limited data exist on the association between vitamin A and iodine. Kimiagar and Vahidi (42) reported from a study conducted in Iran that serum retinol but not  $\beta$ -carotene was significantly lower in iodine-deficient women compared to non-iodine-deficient women. The study concluded that, in iodine-deficient persons, carotene conversion to vitamin A may be disrupted.





• **D**r James Olson (43) presented an overview of dietary carotenoids. He praised a recent review of carotenoids carefully prepared by de Pee and West, which has stimulated great interest among public health professionals.

• Of the more than 600 carotenoids found in nature, only about 50 can be converted biologically to vitamin A. In addition to their provitamin A activity, the recently acclaimed antioxidant function of carotenoids has been associated with reduction of risk for macular degeneration, cataract, cancer, and heart disease. Dietary carotenoids are absorbed in association with lipid, transported via chylomicron to the liver, and later carried by low-density lipoprotein in the circulation. Utilization of dietary carotenoids is influenced by many factors. First, many carotenoids are bound tightly in the essentially fat-free matrix of vegetables, from which they are released with difficulty. In vegetables with large amounts of fiber, carotenoids are usually found in this part. On the one hand, cooking helps to increase carotenoid bioavailability by denaturing protein parts of the matrix, providing a softening effect, and releasing the lipid globules. On the other hand, cooking can also lower bioavailability by enhancing isomerization, oxidative inactivation, and fiber aggregation, which entraps carotenoids. Grinding or pureeing foods usually increases carotenoid bioavailability. For these reasons, Dr Olson recommended that investigators pay more attention to cooking practices.

• Some fat appears essential for carotenoid utilization in order to stimulate bile flow as well as to solubilize the hydrophobic carotenoids in lipid aggregates. Bile acids are required for micelle formation and intestinal absorption of carotenoids. Other dietary enhancers include vitamin E, acting as the antioxidant, as well as a low ratio of saturated fat to polyunsaturated fatty acids. Fi-

ber—in particular, polygalacturonic acid found in pectin—can reduce absorption of carotenoids very effectively, likely through the formation of pectin gels, in addition to the prooxidative effects of iron and copper as well as the competition among carotenoids themselves. Medical problems such as lipid malabsorption syndrome, parasitic infection, and diarrhea markedly lower carotenoid utilization.

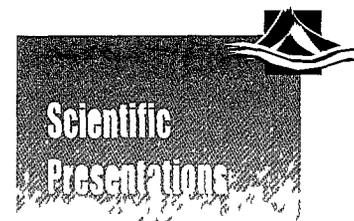
Carotenoids seem to be better absorbed from fruits such as mangoes and papaya and are better utilized in the presence of oil such as red palm oil. However, as dietary carotenoid ingestion increases, intestinal absorption efficiency decreases. Therefore, the nutritional value of carotenoids in relation to vitamin A appears to be influenced by many factors. The widely accepted nutritional value as defined by WHO/Food and Agriculture Organization of the United Nations in 1967 is the  $\beta$ -carotene/retinol ratio of 6:1. Because of the variation effects of factors cited earlier, bioconversion of  $\beta$ -carotene to vitamin A can vary from 2:1 to 10:1. Because of the public health significance of vegetables as sources of provitamin A carotenoids, Dr Olson recommended further investigations to find new ways of enhancing carotenoid bioavailability.

During the discussion period, several issues emerged. The first was that conversion of  $\beta$ -carotene to vitamin A can occur in organs other than the small intestine, such as the liver and kidney. Because of the variation of bioavailability among groups of vegetables and fruits, a conversion range per group rather than a single factor was recommended. The latest study in Indonesia suggested a conversion factor of 10 for yellow/orange fruits and 15 for vegetables. One comment served as a reminder that vegetables and fruits contain nutritive values other than provitamin A carotenoids.

Vitamin A status appears to play a role in bioavailability. Findings of low bioavailability of carotenoid foods are reported in populations with better vitamin A status, primarily adults. The beneficial effect of green leafy vegetables is apparent in VAD children. The question is whether the same effect is seen

among populations with marginal status

The possibility that carotenoids trapped in the chloroplast may not be broken down easily and that other carotenoids such as lutein may be a better indicator of carotenoid intake deserves further attention



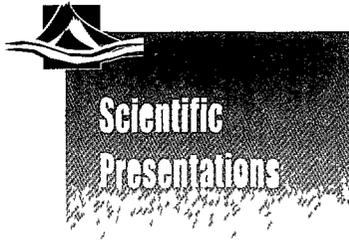
## VITAMIN A FORTIFICATION OF FOODS

**D**r George Purvis (44) opened this plenary session by presenting issues and considerations for fortification of foods. The advantages of fortification are that food grade fortificants are available for most micronutrients and they are compatible with food systems and bioavailable in the foods consumed. The natural dilution factor in food provides a food-related intake and as a result makes excessive intake improbable. Costs are usually lower than those for other delivery systems as they can be incorporated as part of the food cost with an insignificant price increase. Practical constraints exist, however, and must be considered for successful programs. Constraints such as quality issues (primarily flavor and color changes), interactions with food components, and formation of complex compounds should all be easily addressed with the technology currently available. However, private sector involvement and cooperation is vital early in the feasibility evaluation. Virtually all food or food component vehicles are processed or handled by the food industry. Equitable and sound regulations are advantageous and may require refinement to provide equality for food companies. Although costs may be lower than other delivery systems, the program cost relative to benefit needs to be evaluated to allow realistic policy action.

Dr Guillermo Arroyave (45) discussed issues in implementing fortification by reviewing lessons learned from Central American experiences of fortifying sugar with vitamin A. He paid tribute to the role INCAP played in cooperating

with scientists from Hoffmann-La Roche to develop the technology necessary to fortify sugar with vitamin A. In addition, INCAP, as official technical advisor in nutrition to the Central American countries, took the initiative in developing a national program of sugar fortification. This necessitated political, social, and economic considerations and interactions. An important aspect in the success of the program was the lengthy negotiation with the sugar producers, as their unreserved cooperation was needed for achieving the planned objectives, especially in view of the fact that the costs of fortification would be borne by the private sector. In spite of all the negotiations, the first attempt at passing legislation was defeated by a small group of sugar producers still opposing the program. After a second round of negotiations and extensive use of the mass media, fortification legislation was passed. Finally, an important aspect that contributed to the success of the program was that evaluation was built into the program from its onset. The effectiveness of the program in reducing the prevalence of low serum retinol levels has been well documented in the scientific literature.

Dr Roy Tjong (46) presented lessons learned in the development of vitamin A fortification of MSG in Indonesia. A pilot project with vitamin A-fortified MSG showed that it was effective in reducing clinical signs of VAD in preschool children from 1.24% to 0.32% in 6 months. In spite of these promising results, Indonesia was not successful in imple-



menting a national program of vitamin A-fortified MSG. Important points emerged from this experience to ensure the success of fortification. Manufacturers need to support the concept of fortification and the product needs to have the potential of being profitable to the food industry. The government could help the food industry by offering incentives for research and product development and subsidies for the costs involved. Government also needs to be involved in regulating product quality and marketing strategies.

In the discussions that followed the presentations, Dr. Olson pointed out that another problem with the MSG program was the fact that the MSG manufacturers prided themselves on the whiteness and purity of the product and traditionally marketed it in transparent packets. This was at odds with the stability of vitamin A. The product should ideally be marketed in opaque packets, as vitamin A is subject to discoloration. Dr. Max Blum made the point that countries need to

bear in mind that, if there are stability problems with the proposed fortificant, the costs for research and development may render the program economically nonviable.

Concern was expressed that marketing of fortified foods sometimes encourages increased consumption of the vehicle used for fortification. Dr. Omar Dary pointed out that the message provided in Guatemala was not to eat more sugar but to choose fortified sugar rather than unfortified sugar. Nevertheless, the challenge to countries with fortification programs is to pay particular attention to the educational messages given to the public. Dr. Alfred Sommer noted an important issue for consideration in fortification programs, namely, to fortify a food vehicle that is ordinarily eaten by the people at risk. Dr. Tjong pointed out the need for continuous monitoring of the consumption level of the vehicle. As an example, the national consumption of unfortified MSG increased by 58% from 1984 to 1988.

## EXPERIENCES WITH VITAMIN A FORTIFICATION OF FOODS

This session had four oral presentations (47–50) and five poster presentations (51–54), six of the presentations dealt with stability, quality control, and monitoring aspects of sugar fortification. Two posters dealt with the use of  $\beta$ -carotene to fortify staple foods, and one presentation proposed a fortified cookie as a source of vitamin A.

The first oral presentation, by Dr. Rosalinda Hernandez (47), dealt with the Honduran experience in sugar fortification. A three-tier monitoring process was developed that used fortified sugar production quantity projections, chemical analysis, and biological impact evaluation. The constraints encountered in developing the program and the lessons learned were used to develop a set of key issues for sugar fortification programs that incorporate public/private partnership, timely production of premix,

quality control, monitoring, and enforcement.

Dr. Omar Dary (48) presented information on the stability of retinol in sugar when stored for up to 9 months under different environmental and packaging conditions. The half-life was found to vary from 8 to 18 months. Stability was lower in hot, humid conditions. Container size and type did not affect stability. Airtight containers would improve stability but involve additional cost. It was concluded that in order for high-risk groups to receive at least 50% of the recommended dietary allowance for vitamin A, the level of fortification at production should be  $15 \pm 5 \mu\text{g/g}$ .

Dr. Juan Carlos Arraya (52) outlined the strides made by Bolivia to achieve national sugar fortification with vitamin A. He described plans being made to monitor vitamin A levels in sugar.

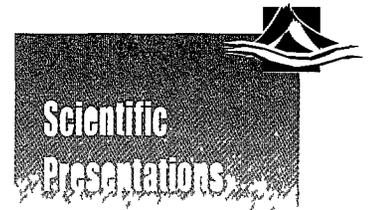
throughout the distribution chain

Mrs Martha Burdick de Piedrasanta (49) presented results of household-level monitoring of salt and sugar samples in Guatemala. The results showed that 62% of the salt samples and 29% of the sugar samples had fortificant levels below the prescribed limit. The speaker identified weak links in the premix, fortification, storage, and transportation system that would need attention to ensure adequate fortificant levels for the consumer.

Dr Monica Guamuch Castañeda (50) reported on the preparation of a nutritious cookie formulated at INCAP to provide vitamin A and other nutrients. The stability of the vitamin A in the cookie after baking and storage indicates

that it could be a cost-effective method to deliver vitamin A to children wherever its consumption could be ensured on a regular and continuous basis.

In the discussion period, it was noted that the monitoring study of fortified sugar was based on a very small number of samples and that there is a need to establish a permanent household monitoring system. Questions were asked about the potential for improving the quality and stability of the fortificant. Dr Max Blum pointed out areas for improvement during fortification, including better adhesive and antioxidant for premix preparation, improved dosing equipment, and selection of the optimal point of premix addition.



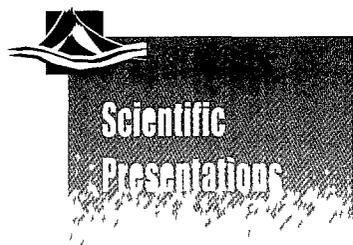
## **BIOLOGIC SIGNIFICANCE OF VAD INFECTION**

This concurrent session on vitamin A and infection consisted of three oral presentations addressing three major types of infections: human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS), acute lower respiratory tract infections, and acute diarrhea. In addition, there were three posters dealing with the impact of vitamin A supplementation on child morbidity and integration of vitamin A with the EPI.

By the year 2000, it is estimated that there will be 40–110 million individuals worldwide infected with HIV. In countries hardest hit by the AIDS epidemic, up to 1 of 10 children may be infected. Previous studies have shown that VAD is associated with increased morbidity and mortality during HIV infection. A major question is whether vitamin A supplementation has therapeutic value for HIV infection. Dr Greg Hussey and colleagues (55) reported the results of a vitamin A clinical trial involving 75 children with AIDS in South Africa. Children were given either 200,000 IU of vitamin A or placebo on 2 successive days. Immune status, as indicated by lymphocyte counts and T-cell subsets, was then measured.

The study showed that, compared with children who received placebo, children who received vitamin A had significant increases in the number of lymphocytes, CD4 T cells, natural killer cells, and memory T cells in the blood 1 month after supplementation. The increase in CD4 T cells is especially important because they are the most commonly used marker for disease progression during HIV infection. In the vitamin A group the CD4 count increased, whereas in the placebo group it decreased. Dr Hussey concluded that vitamin A supplementation increases indicators of immune status in children with AIDS. Clinical outcome data are still being collected. At present, whether vitamin A therapy will improve survival in children with AIDS is still unresolved, but Dr Hussey's study suggests that this approach may be promising. A clinical trial involving 300 HIV-infected children is currently in progress in Kampala, Uganda, to determine whether vitamin A supplementation can reduce mortality in children with AIDS.

The second presentation concerned the potential therapeutic use of vitamin A in children with pneumonia. Dr M. G.



Herrera (for Dr W W Fawzi) and colleagues (56) reported the results of a clinical trial in Tanzania, 625 children with acute lower respiratory tract infection received 200,000 IU of vitamin A or placebo on 2 consecutive days. All children received appropriate antibiotic therapy. They were examined daily for respiratory rate, temperature, heart rate, and oxygen saturation. Vitamin A supplementation had no significant effect on the duration or severity of disease, even after stratification of cases into mild and severe disease. This study suggests that there is no therapeutic benefit of vitamin A on the duration or severity of acute lower respiratory tract infection. The results from the study in Tanzania agree with results of similar clinical trials in Guatemala, Chile, Brazil, and Peru, all of which suggested that vitamin A has no impact on acute lower respiratory tract infection.

The third study addressed the potentially important issue of disease-targeted therapy with vitamin A. Dr Rajiv Bahl and colleagues (57) reported the outcome of a clinical trial involving 900 Indian children with acute diarrhea who received 200,000 IU of vitamin A or placebo and were followed every other day until recovery. Vitamin A supplementa-

tion reduced the risk of persistent diarrhea, and the effect of vitamin A on reduced severity of diarrhea was observed in non-breastfed children. This study supports earlier findings from studies in Brazil and Ghana which suggest that vitamin A supplementation reduces the severity of diarrheal disease.

Poster presentations on this topic included a community-based controlled clinical trial of periodic vitamin A supplementation involving 2500 Indian children (58). In this study, vitamin A supplementation reduced morbidity by 10%. In a study in Sudan, higher dietary intake of vitamin A was associated with increased cough (59), vitamin A supplementation was also associated with increased cough. Finally, a clinical trial involving integration of vitamin A supplementation with the EPI in Bangladesh was reported (60), 250 children received 25,000 IU of vitamin A or placebo with the immunization contacts of the EPI. The investigators found a nonsignificant increase in diarrheal and respiratory infections in the supplemented group.

These six clinical trials have new and provocative implications for research and policy regarding VAD prevention and control.

## DIETARY INTERVENTIONS

This session included 4 oral and 12 poster presentations covering the issues of horticulture and production of vitamin A-rich foods, IEC, food composition tables, vitamin A status and bioavailability, vitamin A intake and morbidity, and food intake methodology.

### HORTICULTURE/PRODUCTION

Talukder and his colleagues in Bangladesh (61) identified crucial elements for the success of home gardening as an intervention for VAD. One important element is to maintain the produc-

tion of at least six varieties of vegetables and fruits throughout the year. Community-based services to provide essential supplies and social marketing to create demand in the general population are also critical. In the long run, the sustainability of the project depends on the possibility of additional earnings through more vegetable production in the communities. The most important message from this study, however, seems to be that it is surprisingly possible to pursue a large-scale home gardening intervention, even in a country noted for its difficult environmental conditions.

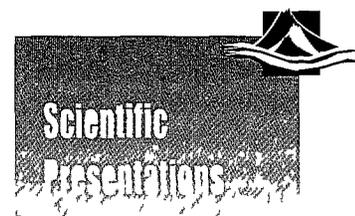
Bloem et al (62) showed that vitamin A intake among women is determined by the variety and production of vegetables and fruits at the homestead. He also showed, through logistic regression modeling, that the poorest households used all their resources for food. Thus, efficacy of home gardening practices as a source for vitamin A intake depends on the behavior of the target group.

Innovative, community-based strategies for increasing knowledge, attitudes, and practices related to production, preparation, and consumption of vegetables were reported from Bangladesh (63) and Kenya (64). Chakravarty (65) showed that horticultural interventions that promote production of vitamin A-rich vegetables and fruits together with effective training, overall community mobilization, and creative IEC actions can improve the availability of vitamin A-rich foods even in some of the most drought-prone areas in India. She found a significant change in consumption not only for vitamin A but also for folic acid and iron when the inputs (e.g., agricultural materials, development of central nurseries, and training) were provided in both the rainy season and winter months.

## INFORMATION/EDUCATION/ COMMUNICATION

Investigators in India (66) who targeted their interventions to preschool children highlighted the importance of processes to create awareness and motivation not only among the target children but also among their mothers and the program's workers and supervisors. A program in Sri Lanka (67) used lecture and interactive group processes to foster changes in the dietary behavior of adolescent girls. The researchers noted the importance of reaching these girls before pregnancy and suggested the feasibility of integrating nutrition education strategies into school health programs.

Findings from the International Eye Foundation's program in northern Guatemala suggested that integration of a variety of creative IEC activities can play an important role in increasing the consumption of vitamin A-rich foods (68). Promotion of home gardens, development of revolving seed funds, and involvement of community leaders as well as mothers have all contributed to the success of the program.



**TABLE 2. FOOD COMPOSITION TABLES**

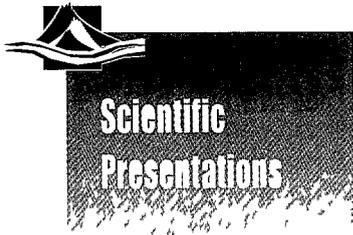
<b>Limitation</b>	<b>Improved Method</b>
Total carotene or $\beta$ -carotene	Provitamin A carotenoids
Analytic losses	Adequate precautions
Influencing factors	Proper sampling
Cooking losses	Analysis of prepared foods

### FOOD COMPOSITION TABLES

Table 2 shows the issues that are related in food composition tables. New data from Indonesia (69) showed that previously published values of provitamin A are too high. The authors recommended that food tables be updated on a continuous and regular basis.

Bhaskarachary et al (70) at the National Institute of Nutrition, Hyderabad, India, analyzed green leafy

vegetables including less familiar and region-specific plants as well as new plant varieties. They showed that  $\beta$ -carotene is the most predominant provitamin A. Some of the newer varieties contain significantly higher concentrations of  $\beta$ -carotene than the traditional varieties. The authors also reported the effects of various cooking methods on the  $\beta$ -carotene content of foods. This information can improve the accuracy of dietary assessment for vitamin A and can en-



hance promotion of appropriate methods of preparation to minimize carotene losses

Takyi and Harrison (71) from Ghana boiled leafy vegetables and used high-performance liquid chromatography to determine resulting  $\beta$ -carotene levels. Some vegetables had a significant reduction in  $\beta$ -carotene after boiling, some had significantly more, and there were no significant changes in others. The authors presented the implications of these findings.

Lopez and Chinchilla (72) also showed that cooking some vegetables reduces the carotene content, whereas in others cooking increases the level. The results suggest that carotene levels increase when vegetables are cooked with oil, but more research is necessary to confirm such a conclusion.

⋮

### VITAMIN A STATUS/ BIOAVAILABILITY

There were three papers dealing with the issue of bioavailability. De Pee et al (73), Bulux et al (74), and Devadas et al (66) looked at the impact of dietary interventions on vitamin A status. Tables 3–5 summarize their results.

The overall conclusion is that lack of bioavailability is a very important issue related to food-based strategies. Although Devadas (66) showed a positive impact of green leafy vegetables on vitamin A status, it is unclear why the high-dose vitamin A supplements had a similar pattern of improvement but were less significant than the vegetables. The data from De Pee (73) and Bulux (74) give food diversification programs the opportunity to identify the best choices of products to promote.

**TABLE 3. CAROTENE-RICH FOODS: THEIR CAPACITY TO IMPROVE THE VITAMIN A STATUS OF CHILDREN**

Vitamin A Source	Impact
Preformed vitamin A foods	+++
Fruits	++
Green leafy vegetables	+
Controls	–

Source: De Pee et al (73). Baseline serum retinol was 0.7  $\mu$ mol/L.

**TABLE 4. IMPACT ANALYSIS OF THE PROVITA PROJECT IN GUATEMALA: LONGITUDINAL RESPONSE OF BIOCHEMICAL MARKERS**

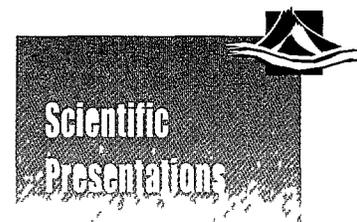
Intervention	Household distribution of vegetables—carrots, sweet potatoes, leafy vegetables
Evaluation	Consumer behavior, biochemical markers
Results	Changes in biochemical markers
Serum retinol	No change (response related to initial level)
$\alpha$ -carotene	Increased (reflect intake)
$\beta$ -carotene	Increased (reflect intake)
Cryptoxanthin	Increased (reflect intake)

Source: Bulux et al (74).

**TABLE 5 DIFFERENT INTERVENTIONS TO IMPROVE VITAMIN A STATUS OF PRESCHOOL CHILDREN IN INDIA**

<b>Intervention</b>	<b>Serum retinol</b>	<b>Xerophthalmia</b>
Green leafy vegetable supplement	+++	Reduction
Green leafy vegetable supplement + education	++++	Reduction
Vitamin A supplement	+	Reduction
Vitamin A + education	++	Reduction

Source: Devadas et al (66). Baseline serum retinol was 17–20 µg/dL. baseline xerophthalmia was 2%–4%



### **VITAMIN A INTAKE AND MORBIDITY**

Bloem et al (62) presented data from Bangladesh and Vietnam. Vitamin A intake above the median was associated with a decreased risk of maternal night blindness. Although the prevalence rates differed between Vietnam and Bangladesh, the odds ratios were similar in both populations. The second observation they presented was a dose-response relationship between vitamin A intake from fruits and vegetables and maternal diarrhea. Again, despite different prevalence rates, the odds ratios were similar and significant after adjusting for possible confounding factors. Interestingly, the association was less striking between the total vitamin A intake (animal and vegetable/fruit sources) and diarrhea. The data may imply that, despite low availability of vegetables, these products still have functional benefits for the consumers.

### **FOOD INTAKE METHODOLOGY**

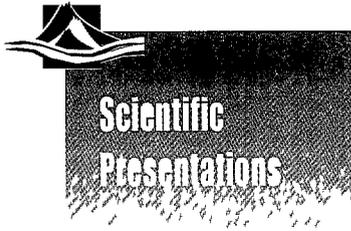
As a part of the Dietvita study in rural Central Java, Indonesia, Ninuk et al (75) quantified the level of vitamin A intake and identified various vitamin A sources in the diets of preschool children. Data were collected for 2 years from 296 children who were 6–47 months old at the start of the experiment. Breast milk was the major source of vitamin A for children less than 23 months old. The primary food sources of vitamin A for

children 24 months and older were eggs, yellow and orange fruits, and green vegetables. Among children over 36 months old, approximately one-half of vitamin A intake came from preformed vitamin A, another one-half was obtained from fruits and vegetables.

Burger et al (76) examined the use of a previously validated food-frequency method to evaluate consumption of vitamin A-rich foods in the regions of Maradi and Tahoua in Niger. A nutrition communication project, using radio and village theatre, was implemented in Tahoua to promote vitamin A-rich foods such as liver, dark green leafy vegetables, and mango. A significantly increased intake of vitamin A-rich food was observed in Tahoua, whereas in Maradi the frequency of intake declined significantly. The increase in consumption of vitamin A-rich foods is consistent with the expected response to the intervention activities in Tahoua. Reasons for the decreased consumption in Maradi will be explored further.

### **SUMMARY AND CONCLUSIONS**

There seems to be general agreement that individuals with access to an adequate food supply can select a nutritious diet from the food available. But for vitamin A interventions, the target population is poor and often lacks an adequate food supply, including vitamin A-rich foods. One way to improve the situation is to increase the effectiveness of foods made available to the poor. In



particular, this will involve identification of appropriate dietary sources of vitamin A and better techniques of food preparation. For poor communities where food markets are not well developed, vegetables would be the main source.

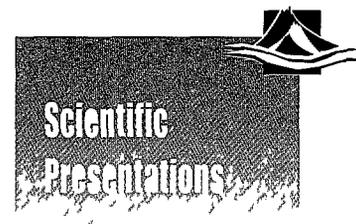
Implementing science for improvement of nutrition is not and will not be simple, especially dietary interventions because of their complexity and less impressive results. If such interventions are considered worthwhile, what can one do to make them better? The knowledge gained from this session suggests the following:

- 1 Home gardens have the potential to improve consumption of carotene-rich foods
- 2 Increased consumption of vitamin A-rich foods reduces the risk of xerophthalmia and maternal morbidity
- 3 Preformed vitamin A is more effective than carotenoid-rich foods in increasing vitamin A status, and fruits seem to be more effective than vegetables
- 4 Processing and cooking result in variable losses of carotene
- 5 Before developing intervention strategies, one must identify the target populations and determine why they have a vitamin A problem. Systemic and holistic approaches to these issues will help improve the effectiveness of intervention
- 6 Before and during implementation, collaboration between all involved should be organized and maintained for maximum effectiveness and sustainability
- 7 If target communities (especially women and children) are well motivated through community mobilization, innovative IEC, training, and adequate support in terms of necessary agricultural materials, the increase of supply and consumption of vitamin A-rich foods is possible. This is true even in areas where vegetable and fruit cultivation practices and physical conditions are poor. The success of this approach likely will depend on the commitment and the ability of change initiators to work together with communities to improve their situation
- 8 If a large-scale program is considered appropriate for a country, the capacity to maintain production of varied vegetables and fruits throughout the year and to manage community-based support should be considered. The success of this approach will depend very much on good program management and the ability to create demand for vitamin A-rich foods not only in the target groups but in the overall population, and, perhaps, with those who have the power to influence changes at a high level
- 9 Where it is feasible, a feeding program should consider giving malnourished children food supplemented with self-produced or low-cost vitamin A-rich foods
- 10 An innovative, well-designed, and well-managed nutrition IEC intervention is essential for a program that aims to increase the supply and consumption of vitamin A-rich foods. An integrated multimedia approach should be considered. It could address what to eat as well as how to obtain the food. It could also motivate people to take appropriate actions
- 11 To improve vitamin A and iron status among adolescent girls as well as prepare them for motherhood, school interventions should offer interactive nutrition and health education. This can assist the target students in obtaining a balanced diet, especially cheap sources of vitamin A- and iron-rich foods, at low cost

## RESEARCH NEEDS

In general, more process-oriented and knowledge-generating research should be conducted as follows

- 1 Learn more about the carotene bioavailability of several types of vegetables under different conditions and identify appropriate methods for maximum retention of carotene during cooking and processing New ways to improve and enhance carotenoid bioavailability in vegetables and other foods will increase the effectiveness of those foods as sources of vitamin A Once new knowledge is gained, effective dissemination of the recommendations is necessary
- 2 Where appropriate, develop small- and large-scale programs and policies to increase the supply and consumption of vitamin A-rich foods
- 3 Where appropriate and necessary, develop effective IEC approaches for community-based and nationwide interventions to promote and advocate vitamin A interventions
- 4 Develop appropriate evaluation methodologies for community-based and nationwide interventions Use realistic and reasonable indicators Use functional parameters for impact analysis of the results



## BIOLOGIC SIGNIFICANCE OF VAD, GROWTH AND INFLAMMATION

Three papers addressed issues related to maternofetal or neonatal vitamin A nutrition. Because vitamin A placental transfer is believed to occur mostly in the third trimester, preterm birth has been associated with poor neonatal vitamin A status. In a poster, Valdes-Ramos and colleagues (77) in Mexico compared differences in cord serum retinol and retinol-binding protein (RBP) in 41 healthy term and 58 preterm neonates as well as in 17 neonates who weighed less than 1500 g at birth and who had been mechanically ventilated for at least 3 days and were, therefore, considered at risk of bronchopulmonary dysplasia.

Compared to term, preterm delivery was associated with a lower birth weight (1095 versus 1736 g), lower serum vitamin A (29.8 versus 33.7  $\mu\text{g}/\text{dL}$ ,  $p < 0.001$ ), and a proportionately lower RBP level (1.2 versus 2.1,  $p < 0.001$ ). High-risk infants, all of whom developed some form of bronchopulmonary dysplasia in the first month of life, had the lowest cord serum retinol level at birth (20.7  $\mu\text{g}/\text{dL}$ ), which remained low during repeated tests over a subsequent 28-day period (at which time mean serum retinol was 14.3  $\mu\text{g}/\text{dL}$ ). The results affirm low vitamin A

status in preterm infants and VAD in very low birth weight infants predisposed to bronchopulmonary dysplasia that persists throughout the neonatal period.

The relationship between intrauterine growth retardation (IUGR) and vitamin A status of mother and newborn was examined by Rondo and colleagues (78) in 356 pairs of mothers and their full-term, single newborns in a case-control study in Sao Paulo, Brazil. Newborns were classified as being IUGR if their weight, obtained within 10 minutes after birth, was below the 10th percentile of a sex-specific weight for gestational age standard, otherwise they were considered to have a birth weight that was appropriate for age. Maternal anthropometry and blood drawing were obtained 12–72 hours after delivery. IUGR newborns were ~3 times more likely than infants with a birth weight appropriate for their age to have a cord serum retinol level  $\leq 0.70 \mu\text{mol}/\text{L}$  (33% versus 15%) despite normal and similar maternal serum retinol levels in both groups of mothers (~1.7  $\mu\text{mol}/\text{L}$ ). There was no correlation between cord and maternal serum retinol ( $r = \text{minus } 0.01$ ), although mean cord serum retinol was roughly



• half that of maternal serum retinol despite the normal vitamin A status of mothers. The authors suggest that the lower cord retinol levels in IUGR newborns could have been a result of inadequate supply, poor binding, increased utilization, or poor storage of retinol during fetal life.

A paper by Christian et al (79) revealed nutritional and health problems associated with night blindness in pregnancy in rural Nepal. In a study of 90 cases and 90 controls, matched by season and reported gestational age, women with night blindness were more vitamin A deficient, anemic, and generally malnourished, with a 9  $\mu\text{g}/\text{dL}$  lower serum retinol level (that is, 21 versus 30  $\mu\text{g}/\text{dL}$ ), a 4-fold higher risk of having abnormal impression cytology in both eyes, a 0.8 g/L lower hemoglobin level, and lower weight and arm circumference. Cases were half as likely to have consumed milk, whey, mangoes, and dark green leaves but were 2–5 times more likely to have eaten non-vitamin A-rich foods such as pale-fleshed gourds and drumstick during the previous week. These differences were observed both early in pregnancy (before they had become night blind) and later after night blindness had become apparent, indicating a diet during pregnancy that was consistently low in vitamin A. Night blindness was also associated with increased risks of lower abdominal pain, painful urination, and diarrhea. Thus, night blindness in pregnancy is an indicator of VAD and is associated with reproductive health risk to the mother.

These three studies reveal the risk of VAD among premature, very low birth weight, and IUGR infants, seemingly irrespective of maternal vitamin A status, but they also provide a first glimpse of previously unknown maternal health and nutritional risks that attend night blindness during pregnancy in a poor rural area of southern Asia, for which the health risks to the fetus and infant remain unknown.

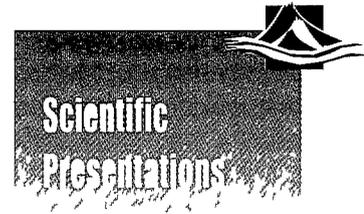
Risk of VAD and acute respiratory infection in the first 5–6 months of life were investigated in a clinical trial by Rahman and colleagues (80) in Bangladesh. They randomly assigned 165 infants (2.5 months old), to receive 50,000 IU of vitamin A or placebo at each of three diphtheria-pertussis-tetanus vaccine (DPT)/oral polio virus vaccine immunizations every 4 weeks. Eighty-five percent of enrolled infants had a low serum retinol level ( $<0.70 \mu\text{mol}/\text{L}$ ) at baseline. Serum retinol testing in 61 infants 1 month after the third vaccine showed significant improvement in serum retinol, although this was more evident in the group receiving vitamin A. At follow-up, 82% (23/28) of infants receiving placebo showed a positive relative dose response (RDR), however, 61% (20/33) of vitamin A recipients were also RDR-positive, indicative of low liver stores. Morbidity assessment in the latter group revealed no differences in diarrheal episodes or cumulative days with diarrhea during the study by RDR status, but infants with an abnormal RDR experienced more frequent acute respiratory infection (40% versus 8%,  $p < 0.03$ ) and twice the number of days of cough with fever (5 versus 11,  $p < 0.05$ ) compared to vitamin A-dosed infants whose RDR was normal. The differences remained significant after adjusting for age, sex, baseline serum retinol, and family income. These findings suggest that a large proportion of infants remain vitamin A deficient even after repeat doses of vitamin A because of frequent respiratory infection accompanied by fever.

Urinary losses of retinol may partly explain the deterioration in vitamin A status with infection in children. Alvarez et al (81) in Peru investigated the extent of serum retinol reduction and losses of retinol in urine of 101 children (1–2 years old) admitted with acute, mild-to-moderate watery diarrhea. On admission, 86% of all children were excreting retinol and RBP. By day 3, 81% of the 52 children still hospitalized were excreting retinol and RBP, 70% (19/27) and 63%

(10/16) were still excreting retinol and RBP on days 4 and 5 of hospitalization. Urinary excretion of retinol was associated with the presence of rotavirus in the stool ( $p = 0.001$ ), a history of fever ( $p < 0.05$ ), levels of several (positive) acute-phase reactants, urinary total protein, and markers of severity of diarrhea such as the presence of glucose, reducing substances, and fat in the stool (all  $p \leq 0.001$ ). Urinary retinol was also inversely associated with the serum transthyretin/RBP ratio, indicating increased renal losses of RBP-retinol ( $p < 0.01$ ). However, although serum retinol decreased with the duration of diarrhea, there was no association between urinary retinol concentration and change in serum retinol from the time of admission, perhaps because of plasma retinol being replenished by the liver. The study adds further evidence of retinol losses through the urine during episodes of watery diarrhea, with implications for potential vitamin A store depletion with repeated infection in early childhood.

Mechanisms of inflammation-induced hyporetinemia were investigated by Rosales et al. (82) in several experiments by injecting an endotoxin (lipo-

polysaccharide) in vitamin A-replete rats and following time-dependent changes in plasma and tissue retinol levels, plasma RBP and transthyretin levels, and levels of RBP and cellular RBP messenger RNA levels. This nonseptic, pathogen-free model avoids the potential confounding effects of preexisting VAD and secondary infection. Lipopolysaccharide-induced inflammation reduced plasma retinol, RBP, and transthyretin levels after 24 hours. These changes were preceded by a 56% reduction in the expression of hepatic RBP messenger RNA (by 12 hours), suggesting that inflammation-induced hyporetinemia is caused by reductions in the synthesis of RBP and subsequent release of holo-RBP into the circulation. These findings support the role of RBP as a negative acute-phase reactant, a response that may be compensatory for sudden increases in hepatic synthesis of other positive acute-phase proteins during inflammation. They also support the argument that an acute-phase reactant, such as C-reactive protein, should be measured in assessing and interpreting serum retinol (which decreases during infection) in human populations.



## USING ETHNOGRAPHIC METHODS IN VAD RESEARCH

At a public health level, the understanding of local culture and environment is essential for planning successful vitamin A intervention programs. Dr Harriet Kuhnlein (83) provided an overview of the development of the focused ethnographic protocol, its field testing in five regions, and a brief summary of the results of field testing. The protocol addresses questions within communities on food availability, vitamin A contents of food, amounts eaten, reasons for eating, and the beliefs and behaviors specific to clinical VAD. Tools included in the protocol were community food system data tables, food frequency and 24-hour recalls, market survey, key informant interviews, belief and behavior

mapping (cognitive mapping) with ethnographic modules, and structured interviews. The field teams tested the protocol at the community level in the Philippines, Peru, Niger, China, and India. In all settings, the teams found that the protocol could be implemented and provided understanding of the local community situation with respect to VAD. The protocol requires from 6 to 8 weeks. Creation of the food system data tables was successful in identifying potential vitamin A-containing foods, many of which did not have identifications or analyses. Some of the important issues uncovered by the protocol include seasonality of vitamin A-rich foods, meal patterns providing clues to finding or



incorporating vitamin A-rich foods, food beliefs and taste preferences, ecological and socioeconomic constraints, people's perception of clinical VAD, and action taken. It is clear that a carefully conducted, short-term focused ethnography can provide essential information for food promotion programs for VAD.

Dr. Lauren Blum (84) provided an in-depth view of ethnographic protocol implementation in two ecologically distinct areas of Hausa communities in Niger. The research method involved key informant interviewing followed by structured interviews. The findings reflect local beliefs and practices for potential health education messages. For example, in both research sites, people believe that the quantity and quality of blood is essential to health. Consumption of blood-rich foods such as liver, red meat, eggs, cow's butter, green leafy vegetables, mango, and carrots, all rich in vitamin A, can return new blood to the body, thus increasing circulation and positively affecting overall health. In Filingue, the northern research site where VAD is prevalent, liver is referred to as medicine for night blindness and the respondents associate VAD symptoms with poor diet, chronic hunger, or removal of breast milk. In contrast, respondents in another site, Mirriah, attributed night blindness to an inexplicable power such as the will of God or a wandering nighttime spirit and were not knowledgeable about food remedies.

The study also examined the effects of structural and economic factors influencing care-seeking behavior. Results indicated that gender roles affect treatment practices, for example, women

are required to request permission from their husbands to conduct activities beyond their daily routine, such as seeking care for xerophthalmia. These findings indicate that men must be a primary target group in any health-related intervention. Overall, the research results demonstrate that an analysis of the food culture and the way people conceptualize clinical deficiency can provide valuable insights into efforts to control VAD.

The discussion period clarified several important issues.

The selection of study areas should take into consideration the prevalence of deficiency in diverse cultures. The key informants were identified by community leaders and usually were those who had lived in the community a long time. The ethnographic approach is not a prevalence study. It represents efforts to find and plan solutions for VAD programs by way of asking the right questions and obtaining the right answers.

There were two poster presentations in this session, and Nuñez and Griffiths (85) reported on El Salvador's nutrition education program. The program employs communication strategies to increase vitamin A intake by young children, pregnant women, and lactating mothers through the use of vitamin A-fortified sugar and the inclusion of vitamin A-rich foods in daily diets.

The study in West Java, Indonesia, by Carlin (86) examined children's food consumption as a form of behavior subject to household customs, food beliefs, and cultural rules for child-parent interaction.

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**D**r Darnton-Hill (87) opened the session by stating that its purpose was to take a critical look at whether vitamin A interventions are sustainable, and if not, why

Dr Bloem spoke for Dr Fasli Jalal about sustainability in the Indonesian context, where it can be defined in three ways. First, the cost of intervention is passed on to the consumer. Second, the government bears the cost and includes it in its budget. Third, the government uses loan money for both economic and human resource development, which includes investing in micronutrients.

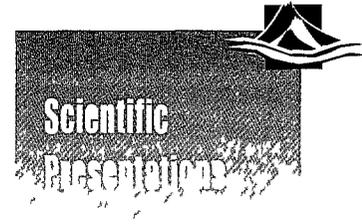
Indonesia has used a combination of medical (supplement distribution), fortification, and food (dietary diversification) approaches to combat VAD over time. Initially, priority was given to distribution of supplements, and the primary emphasis in the food-based strategy approach was to increase energy intake. Once the economic situation improved and the country became xerophthalmia-free, people had more choices about how to use their resources and other interventions for VAD became more feasible. Today the government has broadened its options and is looking at how to break the cycle of VAD. Regardless of the mix of interventions, the underlying key to eliminating VAD is poverty alleviation. Each country must determine not only the most cost-effective mix of interventions but also the optimal use of its loan money. This means that donors must be open-minded about a government's commitment to combating VAD and not try to influence how the loan money is used.

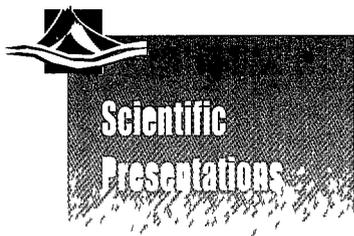
Dr Rabeneck, speaking as a representative of a donor agency, stated that the obstacles imposed by donors result in frustration at the national level. One obstacle is that donors do not listen. They set up labor-intensive procedures for implementing projects, which ignore community needs. This is compounded

by a lack of flexibility in funding arrangements, which means that few donors really have a response mechanism. Another obstacle pertains to overemphasis on measuring results. All too often, the design of a project receives less attention than the measurement of impact. Finally, nutrition is very broad and donor priorities tend to change in terms of both interests and niches. Most donors, however, try to avoid duplicating efforts.

Dr Rabeneck stated that the role and responsibility of international organizations is to provide resources and to work with governments to plan and implement good projects. The private sector is key to creating sustainable programs, but the government has to monitor and provide public education. International organizations must also advocate change at all levels, because the cost of doing nothing exceeds that of the interventions. They should foster innovation, as ideas are needed throughout the process of development, implementation, and monitoring and evaluation. Information concerning what works exists, and the necessary technology exists, but programs do need to be refined.

Mr Venkatesh Mannar commented that international organizations have a vital role working with the scientific community and governments as they can assist with funding and taking corrective action. He also indicated that international organizations need to define the nature and extent of micronutrient deficiencies as well as the options available to different countries, otherwise, governments do not respond. There is also a need to move from short-term to long-term sustainable programs, i.e., fortification and dietary diversification, where the consumer can bear the cost. The international organizations can help create a level playing field for the private sector and can also assist in leveraging funds for governments. This is becoming





- more important as aid is increasingly being given in the form of loans rather than as grants. Finally, international agencies can help with trade issues and technology transfer

Ms Siandwazi (88) spoke of the importance of a south–south dialogue and pointed out that south–south technical cooperation is a sustainable solution because countries are at different stages of development and can learn from each other’s experience. For this to work, however, better use needs to be made of existing opportunities including creating more sustained capacity building, including transfer of skills and relevant knowledge, strengthening the institutional framework for program implementation that includes advocacy for commitment at all levels, and developing an agenda that is more flexible, adaptable, and relevant to local conditions. Programs can be sustainable only if there is a sense of ownership.

- Ms Siandwazi said that part of the process of creating sustainable programs involves forging partnerships with regional centers of excellence. This results in national capacity building for both research and program implementation. Consideration should also be given to strengthen potential centers. Donors and development agencies have a role in supporting south–south technical cooperation as well as in information and data sharing. The sustainability of any program is dependent on its characteristics, i.e., its viability, institutional and human capacity building, and available resources. Local resources must be available when donors pull out.

Ms Churchill commented that the U.S. Peace Corps’ critical concepts for a sustainable project include the following:

- 1 The host government requests assistance
- 2 The program is developed through a decentralized strategic planning process with the community involved

in identifying its needs and developing the solutions

- 3 A multisectoral approach is used
- 4 Counterparts are identified
- 5 The community actively participates
- 6 The use of outside resources is limited and specific. The more resources that are contributed locally, the more sustainable the project. Outside resources are best used for capacity building of community personnel.

Dr Islam described how Worldview International Foundation, Bangladesh, uses the media and individuals in the community to motivate change in dietary habits. He mentioned that collaboration with other NGOs, universities, and donors is important and that 5–6 years of financial support are required.

During the discussion period, Dr Rohde noted the need to engage economists in analyzing the value of investing in nutrition, including micronutrients, because resource allocation is usually determined by the ministry of finance and not the ministry of planning. Dr Rohde advised against focusing on programs that aim at universality rather than those targeted to the people most in need, because VAD is most prevalent in areas that are remote and difficult to reach.

Dr Ismail pointed out that community participation has been discussed for decades, but it still seems to mean that the community is informed rather than that it participates in identifying its priorities. A vicious cycle exists, because donors want to know what the program entails, but until the funding is available community assessments cannot be implemented. Dr Ismail said there are examples, and not just in developed countries, of sustainable nutrition interventions that have come about because of support at all levels, including training at the regional level.

Dr Kavishe noted that there are three issues that cannot be ignored when considering sustainability. The first is capacity building in research, training, and

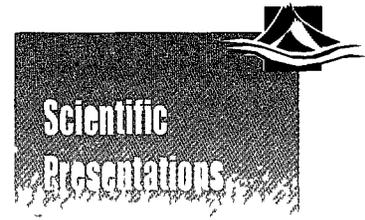
program management This includes linking institutions Program outcomes and processes are equally important, and this should not be overlooked Second, there is a need for a mix of interventions within the country context (e.g., immunization against measles has had a big impact on xerophthalmia) Third, there are complementarities in the approaches used for the different micronutrients Dr Aguilar noted that we are in the era of global communication, thus, networking at regional and international levels is essential

Dr Keith West commented that although program agencies know how to evaluate program processes and outputs, they do not know how to evaluate program outcomes or impact This design issue tends to result in confusion

in interpreting program performance To overcome this problem, national institutions should be developed so that they are more skilled in impact evaluations

Mr Clay noted that sustainability is often mistakenly interpreted as meaning cost-free The key is to develop and build systems within programs that governments and communities can afford to maintain All too often, the long term is interpreted to mean "nothing needs to be done now" but, in order to maximize the return on investment, action is needed now

Ms Godínez mentioned that there is a need to look carefully at how programs and projects are operationalized All too often there is a dependence on volunteers, which may not be appropriate for ensuring sustainability



## OTHER INTERVENTIONS FOR PREVENTION AND CONTROL OF VAD

In this session, there were four complementary oral presentations: one on the safety aspect of vitamin A administration to low-birth-weight infants, one on the influence of parasites and the impact of deworming on vitamin A status, and two on the vitamin A supplementation program in Bangladesh

Dr Frank Chytil (89) summarized work on the use of vitamin A in improving the health and survival of very low birth weight infants born in the United States. Blood levels of vitamin A in low-birth-weight infants were found to be low, and the lungs of very low birth weight infants who died showed squamous hyperplasia similar to that found in vitamin A-deficient animals. Because of these observations, trials were carried out to determine whether giving such children additional vitamin A improved their survival. Vitamin A appears to be very important for development and functioning of the lungs of very low birth weight babies. For these babies, 2000 IU of vitamin A per kg of water-miscible retinyl palmitate was given by intramus-

cular injection every 2 days. Side effects were closely monitored by measuring serum retinol, bulging fontanelle, and vomiting. The dose was found to be well tolerated. Workers in South Africa had found that 7500 IU per baby was also well tolerated. Evidence was presented that this vitamin A dose improved one measure of lung function. A multicenter trial is under way to investigate the benefits of intramuscular administration of vitamin A to premature children. Since 1986, more than 350 very low birth weight neonates were given vitamin A in the Vanderbilt University Medical Center intensive care unit. Signs of acute toxicity were not observed in any patient.

Dr James Tielsch (90) presented an intervention study that was done in Zanzibar in about 400 school-age children. This is a part of a large community trial in school-age children to look at ways of controlling parasites and improving health. Schistosomiasis is already partly controlled, but most other parasitic infections, including malaria and worms, are very common. The baseline



data showed poor nutrition status 40% of children were stunted and anemia was detected in 82% of children. However, vitamin A status as represented by serum retinol and modified RDR (MRDR) was very good. Mean serum retinol was 35 µg/dL, and no children exhibited a level less than 10 µg/dL. Distribution of serum retinol was similar in children in the United States of the same age. The study found no association between any type of worm (*Ascaris*, *Trichuris*, or hookworm) or with malaria or schistosomiasis and vitamin A status. All children were dewormed. The follow-up after 1 year showed a slight decline in serum retinol concentrations. There was no association of *Ascaris* or *Trichuris* infection at baseline with change in serum retinol or of helminthic infection with change in MRDR. However, there was a small association of serum retinol level with hookworm, because treatment of children with intense infections eliminated the decline in vitamin A status. The investigators concluded the following:

1. Communities exist on a tropical African island where vitamin A status is good without intervention. The authors speculate that this is because of consumption of whole, small fish on the island.
2. Good vitamin A status can coexist with poor iron status and parasitic infection.
3. Where vitamin A status is good, reducing geohelminths has little effect on vitamin A status.

In the discussion period, a participant said there was enormous literature from several countries that showed deworming did have a beneficial effect on immunity and growth. Dr. Tielsch agreed and said that some of these effects had been seen in Zanzibar, but he had limited his presentation to the effects of deworming on vitamin A status, and little effect had been expected because the vitamin A status was already good. This was not known, however, before the study started.

Dr. Mohammed Shahjahan (91) reported on the integration of vitamin A supplementation with the EPI in Bangladesh. In 1979, after recognition of widespread VAD, the government of Bangladesh introduced a program aimed at giving all young children vitamin A capsules. Capsules were to be provided through home visits and outreach services. After 10 years of implementation efforts, only about one-third of the eligible children had received vitamin A. However, EPI coverage was much higher than this, over 80% of children received Bacillus Calmette-Guérin and DPT vaccines. Moreover, there was a strong political commitment to immunizing all children, and a good monitoring system existed. In 1990, vitamin A supplementation was formally combined with EPI and given the name EPI Plus. Intensive training and social mobilization took place and a monitoring system for vitamin A was established. Vitamin A capsule coverage went up to approximately 80% of all eligible children in both 1994 and 1995. In Bangladesh at the present time, 25,000 IU of liquid vitamin A from an oral dispenser is given to infants together with DPT1, DPT3, and measles immunizations. Integration improved coverage and cost-effectiveness, and the results were much better than when two separate programs were conducted.

Dr. Abdul Hye (92) gave further details of the Bangladesh vitamin A capsule program and how it was monitored. He described a large, ongoing multipurpose nutrition surveillance system. The presentation showed how the nutrition surveillance system could be used to monitor distribution of vitamin A capsules. The monitoring system showed clearly the dramatic decline in capsule coverage when a donor withdrew vitamin A capsules and the increase in coverage once an alternative donor was found. The combined EPI/vitamin A capsule distribution program became even more effective once the decision was made to implement a National Immunisation Day in April 1995, and the

monitoring system was able to provide information to planners about the programs. The problem with immunization days is that they are often held only once a year whereas vitamin A capsules should be distributed twice a year. In Bangladesh, a separate National Vitamin A Week was organized. During this time, special efforts were made to provide all children with vitamin A capsules as well as to promote breastfeeding and knowledge of diarrhea treatment. The surveillance system showed that this was highly effective. The National Vitamin A Week proved to be a highly effective, low-cost way to maintain coverage. Coverage of over 80% on immunization days and over 70% during National Vitamin A Week was achieved. The surveillance program produces very detailed data, e.g., it shows that capsule coverage for boys and girls is similar, it allows planners to focus on particular districts that have low coverage, and it shows that the program is reaching the most vulnerable groups—the very poor and children of parents with little education. Unlike many nutrition surveillance systems, the data collected in Bangladesh are fed back rapidly to decision makers and used to influence action, 60,000 copies of the results of the vitamin A capsule distribution program are distributed to local planners.

In the discussion period, Dr. John Clements of WHO felt it would be possible to link capsule distribution with polio eradication in many countries. Once polio is eradicated, mass campaigns would still be used for measles. One participant questioned why supplements were given to young infants instead of to their mothers immediately after birth. The response was that this activity is being planned in Bangladesh. The merits of supplements given to young infants were discussed. Dr. Keith West summarized the data on safety and mentioned the meta-analysis on vitamin A and acute respiratory infection that has just been published. There was a fair amount of evidence that vitamin A decreases diarrhea. A study in Indonesia showed a two-

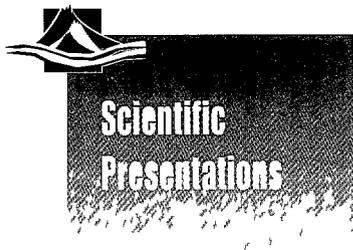
thirds reduction in mortality when a supplement was given to infants at birth, but another study in Nepal showed no impact on mortality. Another participant stressed the enormity of the achievement of ensuring that over 80% of Bangladeshi children now receive vitamin A capsules and that, although the supplement regimen used in Bangladesh was different from that used in most other countries, the government of Bangladesh was correct in not trying to constantly change this nationwide program on the basis of the results of any particular small study.

The poster presentations consisted of two papers on multiple approaches of the vitamin A program: one on the effects of supplementation together with deworming and one on vitamin A inhalation.

Villate et al. (93) described the achievement of the combined approaches of vitamin A supplementation and nutrition education in the Philippines. The program was planned to test the impact of different interventions—radio, comic books, mothers' classes, and counseling in addition to vitamin A supplementation. Mass capsule distribution took place in 1993, and 86% of children (1–5 years old) received capsules in the expanded program. The baseline survey was conducted in 1991 and the evaluation survey was carried out in mid-1994 with 11,000 preschool children. The results indicated that night blindness declined to 1.0% in all four intervention groups. Low weight for age declined in all groups except the radio group.

Calderon (94) described a program that supports improved dietary intake of vitamin A from animal and vegetable sources and targets capsules to young children and mothers after birth. The project works predominantly in rural communities of difficult access, strengthens institutional coordination, and increases coverage through participation of the Ministries of Health and Agriculture as well as the NGOs. Another important component is the sustainability intervention of community groups by initiating cost recovery activi-





ties such as selling of vegetable seeds by health promoters and agricultural representatives. A model farm was established in the target communities to improve the family nutritional status.

Tanumihardjo et al (95) presented the results of a vitamin A intervention study of 309 Indonesian children known to have *Ascaris lumbricoides*. Six different treatments, including a 210- $\mu$ mol vitamin A supplement and a 400-mg dose of the deworming medicine albendazole, were randomly administered together or at different times during a 1-month period. Vitamin A supplements—but not albendazole—improved vitamin A status as assessed by MRDR. Vitamin A and albendazole given together also improved vitamin A status. The MRDR test proved a better discriminator of the treatment

effects on vitamin A status than did changes in serum retinol values.

Biesalski (96) described an experiment with vitamin A inhalation. The rationale was that in the presence of diarrhea, severe protein-energy malnutrition or VAD, vitamin A may not reach the target tissue, especially the epithelium of the respiratory tract. The experiment showed that rats could absorb retinol by inhalation, and it went to the respiratory epithelium. Adult volunteers inhaled 3000 IU of retinol, and plasma retinyl esters increased after 30 minutes, with no side effects. This may be a promising way to facilitate organ-specific targeting of vitamin A. In the discussion, it was noted that oral doses of vitamin A are still absorbed, albeit at a lower level, and inhalers are likely to be expensive.

## VITAMIN A STATUS METHODOLOGY

### BREAST MILK RETINOL

Dr Kjolhede (97) presented work demonstrating that small casual samples of breast milk can be reliably used to assess milk retinol concentration if the vitamin A content is expressed in terms of fat content. Lactating women living in the Matlab area of Bangladesh were randomized to breast milk collection by either “full” or “casual” sampling. Full sampling was done from a breast that had not been used to feed a baby for at least 2 hours, and a manual pump was used to collect all the milk in the breast. Casual sampling was done by manually expressing 5–10 mL of milk from a breast regardless of how recently it had been used to feed a baby. For both samples, measurement of the amount of cream in the specimen was obtained, and the sample was divided into aliquots, sent to the laboratory in Dhaka, and kept at 4°C before being analyzed by high-performance liquid chromatography the following day. When the vitamin A content was expressed per g of milk fat, there was no significant

difference between sampling methods in the vitamin A concentration of the milk or in the proportion of samples that were classified as deficient ( $<1.05 \mu\text{mol/L}$ ). Thus, breast milk sampling can be done successfully in women’s homes in the field and only casual samples need be collected, provided the fat content is measured and vitamin A concentration is expressed per g of milk fat.

De Pee et al (98), however, presented data showing that, in some cases, breast milk retinol expressed per unit volume is a more responsive indicator than breast milk expressed per g of fat. Two important factors seemed to affect this. First, in the population they studied there was a wide range of time since delivery of the breastfed child (e.g., a wide range in stage of lactation). This would result in a large standard deviation (SD) around the mean milk retinol concentrations before and after the intervention because milk retinol varies a great deal from early to late lactation. Second, the intervention (a  $\beta$ -carotene-fortified wafer) increased the

fat as well as the retinol content of the breast milk among supplemented mothers. Thus, retinol expressed per unit volume measured the combined response of both the fat and the vitamin A, so that this indicator showed the greatest response and required the smallest sample size to detect a difference. This study also demonstrated that both the fat and the retinol concentration increase in breast milk as lactation ensues (e.g., as the baby grows older), that 26% of women who had serum retinol levels less than 0.70  $\mu\text{mol/L}$  remained MRDR negative, and that, for a given MRDR ratio, breastfeeding women had a significantly lower serum retinol level compared to non-breastfeeding women.

### **RESPONSE TESTS**

Two papers were presented in which a response test (MRDR and RDR) was used to assess adequacy of the vitamin A stores of infants and children in Bangladesh and India. Using the RDR test, Dr. Wahed and colleagues (99) demonstrated that 64% of apparently healthy infants presenting for immunizations at the International Centre for Diarrhoeal Disease Research, Bangladesh, had low liver reserves of vitamin A (RDR  $\geq 20\%$ ). This showed that, even among young infants, VAD is prevalent.

In a group of 24 undernourished children living in an orphanage, investigators in India used the MRDR to assess improvement after either daily retinyl palmitate or red palm oil supplementation for 60 days (100). Dr. Raghuramulu reported that after the intervention, the MRDR ratio fell dramatically and all children had a value less than 0.046, the cutoff identified by the investigators as being appropriate for defining adequacy based on regression lines and the point of intersection. They concluded that the MRDR was a good indicator of subclinical VAD in their population.

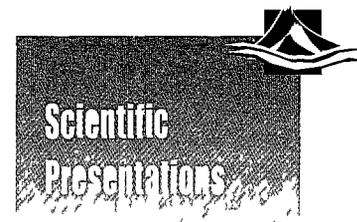
### **BIOCHEMICAL INDICATORS OF FOOD COMPOSITION AND FOOD CONSUMPTION**

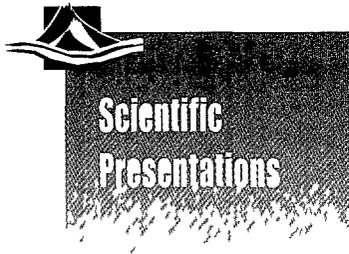
Dr. Thurnham (101) suggested that plasma lutein may be an excellent marker of vegetable intake. Lutein is present in most vegetables (but not in fruits) in approximately the same amount as  $\beta$ -carotene. Unlike  $\beta$ -carotene, lutein is not converted to vitamin A, so it is a better marker of intake. In this report, the investigators measured lutein, retinol, and  $\beta$ -carotene in the plasma of Pakistani infants before and after the summer season, when vegetables are plentiful. At the end of the season of plenty, all measures increased, but not significantly so for  $\beta$ -carotene. After the season of plenty, plasma lutein, but not plasma  $\beta$ -carotene, was significantly correlated with plasma retinol concentration. In addition,  $\beta$ -carotene was undetectable in more than 68% of samples.

Dr. Lietz (102) presented a method for measuring carotenoid and tocopherol in palm oil by using a microbial lipase instead of saponification to hydrolyze fatty acids. The saponification step often results in significant losses of these analytes. The work showed excellent results, with far less loss by this proposed method.

### **MATERNAL SERUM AND CORD BLOOD RETINOL CONCENTRATION AS AN INDICATOR OF INFANT VITAMIN A STATUS AND HEALTH**

Dr. Gorodischer (103) reported results of a cross-sectional study in which 313 apparently healthy mother-infant pairs were assessed for maternal serum retinol and cord blood retinol. Low serum retinol was prevalent among mothers and infants. Compared to mothers with serum retinol concentrations  $\geq 20 \mu\text{g/dL}$ ,





a greater proportion of mothers with serum retinol concentrations below this cutoff gave birth to infants of shorter gestational age and of lower birth weight

### **VITAMIN A CONCENTRATIONS MEASURED IN DRIED WHOLE BLOOD SPOTS**

Work carried out by Humphrey et al (104) demonstrated that retinol (as holo-RBP) can be accurately quantified in 1–2 drops of whole blood, collected and dried on filter paper, and analyzed by high-performance capillary zone electrophoresis. Although most of the samples analyzed by high-performance capillary zone electrophoresis agreed closely with values obtained by conventional high-performance liquid chromatography, about 10% of the samples showed poor agreement. Work is under way to overcome this remaining challenge. The investigators also demonstrated that holo-RBP was stable in blood spots when stored at  $\leq 4^{\circ}\text{C}$ , but not at room temperature, and when stored at 30% humidity, but not at 90% humidity. There was moderate loss when samples were subjected to either 8 hours of room light or 4 hours of direct ultraviolet light. The authors suggest that samples be protected from direct light while drying and then stored in a Ziplock plastic bag as soon as possible in either the refrigerator or the freezer.

### **STABLE ISOTOPE TECHNIQUES TO ASSESS LIVER STORES OF VITAMIN A**

Dr Haskell (105) presented work validating the deuterated retinol dilution technique of estimating total body stores of vitamin A against measurement of vitamin A concentration in a liver biopsy sample among VAD subjects. When three patients with clinical histories consistent with poor absorption or retention of the vitamin were omitted from the analysis, the linear correlation between the two techniques was very good ( $r = 0.82$ ). The deuterated retinol dilution technique

appears to be promising for population assessment and for evaluating the impact of interventions on vitamin A stores. It is the only technique for indirect assessment of vitamin A reserves in the liver currently available.

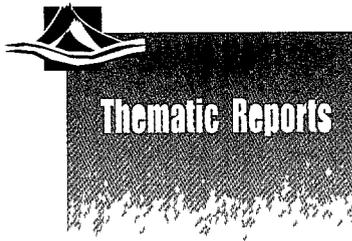
### **SERUM RETINOL CONCENTRATION**

Serum retinol was used to assess vitamin A status in a survey carried out in the Marshall Islands (106). Eight percent of the 800 preschool children in the study were found to have retinol levels less than  $0.35 \mu\text{mol/L}$ , and a startling 55% were found to have levels of  $0.35$ – $0.70 \mu\text{mol/L}$ . Simultaneously, a VAD risk assessment questionnaire was administered to a subsample of the children's parents. The authors concluded that serum retinol concentration is a very informative indicator for population assessment. They also found that the VAD risk assessment questionnaire was valid in comparison with serum retinol and could be a valuable method for surveillance in the Marshall Islands.

### **DIETARY ASSESSMENT METHODOLOGY**

The HKI semiquantitative food frequency questionnaire (FFQ) and the HKI qualitative assessment of VAD were used to quickly determine whether VAD was likely to be a problem in a rural village in India (107). If cow and breast milk were not included in the questionnaire, in keeping with HKI recommendations, the mean frequencies of consumption of vitamin A were below 4 times per week for animal sources and 5 times per week for weighted sources, which are below the suggested cutoffs for a high-risk community. Vitamin A capsule coverage was poor (63%) and Bitot's spots were prevalent (4.3%). The authors concluded that the rapid assessment techniques recommended by HKI were useful in demonstrating that deficiency was likely to be a problem and in providing some





Three experts were invited to summarize the meeting information on population assessment, biologic significance of VAD and marginal VAD, and appropriate interventions

## POPULATION ASSESSMENT

Dr Jean Humphrey (109) began by stating that children with subclinical VAD who appear to be healthy are more likely to die before their 5th birthday compared to children with adequate vitamin A status. The challenge now is to identify these children and the communities where they live. This summary will try to answer the following questions

- 1 What indicators of vitamin A status are we using?
- 2 What have we learned about their sensitivity, reliability, and responsiveness to interventions at this IVACG meeting?
- 3 What can we recommend about assessing vitamin A status and what are the gaps requiring future research?

At this meeting, 58 presentations assessed human vitamin A status with one or more indicators. One paper reported experience with deuterated retinol and liver biopsy, and three papers used conjunctival impression cytology. Of the 18 papers reporting dietary data, most used a FFQ. Fifteen studies reported xerophthalmia rates in children, and four presented night-blindness rates in women. Lutein was proposed as a new method in one paper, whereas carotenoids and RBP were measured in several studies. Of the eight papers reporting response test data, six used the MRDR. Finally, 40 of the 58 studies had used serum or plasma retinol concentrations as an indicator of vitamin A status. Obviously, the major message from this distribution is that despite all its limitations, serum vitamin A is still the indicator of vitamin A status that is by far the most commonly used by the vitamin A community.

## Serum Retinol

In her global status review, Dr Underwood described serum retinol concentrations as "the best available indicator for which the most data has been collected," and because of this, the prevalence of serum retinol concentrations  $< 0.70 \mu\text{mol/L}$  or  $< 20 \mu\text{g/dL}$  is now the basis of the system for classifying countries as having a public health problem. However, several presentations at this and previous IVACG meetings have cautioned about the interpretation of serum retinol levels in individuals with concurrent infection and in populations known to have a high prevalence of many infections.

Dr Alvarez's presentation showed that, even in acute afebrile episodes of diarrhea of only 4–5 days duration, serum retinol may drop by 20%–30% (81). Dr Rosales's (82) elegant rat model suggests that inflammation results in a very rapid reduction in hepatic synthesis of RBP, with a subsequent drop in circulating retinol levels. In a national sample of children in Nicaragua, serum retinol concentrations were *not* associated with vitamin A intake, but they were significantly associated with recent illness, especially fever (33). In a hospital-based study in India, serum retinol levels were lower in children with diarrhea and acute respiratory infection compared to age-matched controls (58). Clearly, in people with concurrent or recent infection, serum retinol is not a reliable indicator of vitamin A status.

As there is increased interest in targeting vitamin A interventions to people who are infected, or at high risk of infection, and especially as there is also interest in assessing the vitamin A status of populations, of whom 20%–30% may be infected with HIV in addition to the normal rates of other infections, it is critical to learn how to assess vitamin A status and interpret serum retinol concentration in infected people. We need something akin to the human transferrin receptor recently developed by those working with iron.

Several suggestions have been made for studying serum retinol. First, samples analyzed for retinol should also be analyzed for an acute-phase protein. Although no single acute-phase protein perfectly reflects the severity and duration of an episode of infection, acid glycoprotein,  $\alpha_1$ -antichymotrypsin, and C-reactive protein were all suggested at this meeting. It is not clear how these acute-phase protein values would be used. One creative person suggested that different cutoffs for VAD might be established for people with elevated acute-phase proteins. At a minimum, it would seem prudent to measure temperature and elicit a brief current and recent morbidity history when drawing blood for serum retinol analysis.

Collecting and transporting serum for retinol analysis presents logistical constraints. It is possible to analyze vitamin A in 1–2 drops of whole blood collected and dried on a piece of filter paper (104). Resolving the remaining technical problems should greatly ease the burden of collecting blood samples, especially in community-based surveys.

### **Diet**

As a reminder, it is known that dietary assessment does not assess vitamin A status, but it does assess an important determinant of vitamin A status.

The FFQ, either as part of the IVACG Guidelines for Simplified Dietary Assessment or the 7-day semiquantitative FFQ developed by HKI or an unspecified FFQ, was the most popular tool used by meeting participants to measure food intake. Several papers reported success with this tool.

FFQs were used to document a statistically significant increase in consumption of vitamin A-rich foods after a nutrition education intervention (67), to document a statistically significant increase in consumption of particular foods promoted through a radio, theater, and home-gardening intervention package (76), and to document the fact

that nonxerophthalmic control children had greater dietary diversity compared to xerophthalmic children (73).

Whereas a FFQ was useful in identifying major sources of vitamin A in an Indonesian diet, the absolute amount of vitamin A consumed estimated by the FFQ was nearly double that of the weighed food intake (108). This has been commonly reported from FFQ—especially those with fairly long food lists. The longer the list, the more likely intake will be overestimated.

The mean of 24-hour dietary histories has often been suggested as a good way to estimate the average daily intake by a population. Thus, it may be best to do both a food frequency and a 24-hour diet history as they may have complementary strengths.

Presentations highlighted the fact that many food composition databases are based on outdated laboratory methods. For example, recent laboratory analyses showed that the provitamin A contents of many foods listed in Indonesian food composition books were outdated and greatly overestimated (69).

Finally, there is the “hot” area of differential bioavailability of the carotenoids in different fruits and vegetables as a result of poorly understood differences in the vegetable matrix, preparation methods, and composition of the meal within which the provitamin A food is eaten (43). It appears that the nutritional ratio for provitamin A/retinol activity may vary considerably from one fruit or vegetable to another. In the name of simplifying dietary assessment, perhaps provitamin A foods with similar carotenoid/vitamin A activity ratios could be grouped together. A lot of hard work must be completed before there is an adequate understanding of this issue, but the effort has been started by Drs. de Pee and West. Their initial work suggests that the nutritional ratio for deep yellow to orange fruits is 10 and that for dark green leafy vegetables is 15—both factors considerably greater than the conventional factor of 6.





### **Response Tests (RDR and MRDR)**

The RDR assay was originally developed and validated by Drs Underwood, Campos, and colleagues based on their insightful understanding of the differences in utilization of ingested retinol by deficient and sufficient subjects. It was then modified by Drs Tanumihardjo and Olson to increase feasibility by eliminating one of the two blood draws. Both of these tests continue to be well-accepted methods of assessment when an investigator wants to estimate the proportion of people with depleted liver vitamin A stores in a relatively small number of subjects. They are also used to assess the effectiveness and duration of an intervention, and frequently they are used to assess a representative subset of subjects in a population-based survey in which a less expensive, but also less sensitive, indicator (like eye signs) is used in assessing the entire population. Several studies presented at this meeting considered the use of these methods in children with infections (80, 90, 95).

In discussions about assessment, there are always attempts to decide which is the "best" indicator. At this meeting, there was a lot more sophisticated discussion about which indicator was the most "sensitive" and which was the most "responsive" to interventions. Sensitivity is the number of truly deficient people who are abnormal by a test divided by the number of truly deficient people. To calculate real sensitivity, one must know who is truly deficient, which is, of course, what we set out to do in the first place.

In many discussions, it was said that serum vitamin A was more sensitive than RDR because the number of people with serum values below  $0.7 \mu\text{mol/L}$  was greater than the number who tested positive for RDR. This presumes that everyone with serum vitamin A below  $0.7 \mu\text{mol/L}$  is truly deficient, however, as mentioned earlier, there is overwhelming evidence that infection and no doubt many other factors can result in low serum vitamin A levels that do not reflect deficiency.

Response is the change in an indicator before and after an intervention divided by the average SD of the two estimates. The greater the change, and the smaller the variability around the estimates before and after, the greater the responsiveness of an indicator.

For example, in comparisons of the mean serum retinol and SDs of serum retinol and MRDR ratios in children supplemented with vitamin A or red palm oil, serum retinol was nearly 3 times more responsive than the MRDR (100). But, in another study, the observed change in serum retinol was very small compared to the change in MRDR, so the MRDR was 35 times more responsive than serum retinol (95). These results show that no single indicator is superior to another.

When choosing and interpreting indicators, one should remember that many factors influence their performance, including the level and heterogeneity of deficiency of the population being assessed, the intervention being evaluated, and the analytic precision attained in the laboratory.

### **Breast Milk Vitamin A Concentration**

Breast milk is a readily available fluid that can be collected noninvasively. Experience by presenters at this and previous IVACG meetings suggests that breast milk sampling is acceptable to women in several different cultures—indeed women are often keen to know the "quality" of their milk. Finally, vitamin A in breast milk is an indicator for two vulnerable groups—lactating women and their infants.

One of the difficulties of measuring vitamin A in breast milk is that the vitamin A is found in the fat portion of the milk, and the fat content of milk varies tremendously in the same woman according to time of day, the beginning and end of a single feeding, time since the breast was last used to feed an infant, and age of the infant. Therefore, in the past, it was thought that one needed to

control for time of day, to collect milk only from a breast that had not been used to feed a baby for at least 2 hours, and then to collect all the milk from the breast. At this meeting, it was learned that small casual samples of milk can be reliably used if the vitamin A content is expressed in terms of fat content. This means that breast milk sampling can be easily performed in the field in a woman's home (97).

In addition, in some cases, breast milk expressed per volume may be more responsive than breast milk expressed per g of fat if the intervention being evaluated also increases breast milk fat content (98). The heterogeneity of the time since delivery of the woman being assessed also influences the responsiveness of milk (milk retinol changes a great deal over lactation), if women at many different stages of lactation are being assessed, the variation between them in milk retinol levels will be large, reducing the responsiveness of the indicator. If the group of women being assessed are all at the same stage of lactation, the variability between them will be smaller and the responsiveness of breast milk vitamin A may be larger.

### ***Clinical Signs and Symptoms, Especially Among Women***

At the last IVACG meeting, Dr. Martin Bloem reported that, in Bangladesh, night blindness in pregnant women was more prevalent than xerophthalmia in preschool children. At this meeting, there were four reports related to maternal night blindness (24, 25, 62, 79).

Clearly, maternal night blindness is a prevalent problem that has been overlooked. In addition to identifying women who may be at increased risk of morbidity and mortality, maternal night blindness may be a good marker of households and communities where children are likely to be at risk for developing xerophthalmia even before they show measurable signs of deficiency and most

immediately for populations in which infants are likely to receive inadequate amounts of vitamin A through breast milk.

Several issues remain to be resolved. Although clear associations have been noted between measures of vitamin A status or dietary intake and maternal night blindness, it has not been clearly documented on a population basis that maternal night blindness responds to vitamin A supplementation. It may well be that maternal night blindness is multifactorial in nature.

Night blindness in preschool children living in areas where a specific term for the condition exists has been shown to be a highly sensitive indicator of VAD. In the same way, the sensitivity and specificity of maternal night blindness in detecting VAD among women needs to be defined.

In conclusion, marginal vitamin A status is difficult to measure. However, this is the very same level of deficiency that may result in the deaths of over a million children a year. Efforts must be renewed to identify these children early and avert these preventable deaths.

### **BIOLOGIC SIGNIFICANCE OF VAD AND MARGINAL VAD**

Dr. Greg Hussey (110) provided a summary of the numerous oral and poster presentations related to the biological significance of VAD and marginal VAD. The presentations can be divided into four themes: 1) vitamin A and infection (AIDS, acute respiratory infection/diarrheal disease, parasitic infection), 2) vitamin A and growth, 3) vitamin A and micronutrients (anemia, iodine deficiency disorders), and 4) risk factors and mechanisms of VAD. Where appropriate, each section is discussed under the following headings:

- 1) What was the knowledge base before this IVACG meeting?
- 2) What new information has been learned?





- 3 What were the major concerns, if any, raised at this meeting?
- 4 What are the recommendations in terms of policy and research that have arisen during the course of the meeting?

### ***Vitamin A and Infection***

*HIV/AIDS* Over the past few years evidence of a significant association between vitamin A and HIV infection has emerged. In adults, VAD is associated with reduced immune competence, increased morbidity and mortality, and increased perinatal transmission. In addition, vitamin A supplementation in infants has been shown to reduce morbidity.

The single paper presented on AIDS in children indicated that there is a positive correlation between vitamin A status and CD4 counts and that children with severe disease have lower vitamin A levels (55). In addition, high-dose vitamin A supplementation significantly improved vitamin A status and enhanced immune function.

The major concern relates to the safety of vitamin A in HIV-infected persons. This is based on *in vitro* evidence that vitamin A increases viral replication. The limited available clinical data, however, do not support this laboratory finding.

The question that many people have asked is, Should vitamin A therapy be advocated in children with AIDS? At this stage, it cannot be prescriptive. Additional research evaluating clinical efficacy and the role of other micronutrients and their interaction with vitamin A is needed. Hopefully the current vitamin A clinical efficacy trial in Uganda and studies evaluating the impact of vitamin A on viral load will help resolve some of these concerns.

*Acute respiratory infection and diarrhea diseases—effectiveness studies* It is well recognized that VAD is associated with increased morbidity and mortality after

measles, acute respiratory infections, and diarrheal diseases. Community-based intervention studies have shown that childhood mortality (in those over 6 months old) is reduced 25%–30%. Vitamin A therapy also reduces morbidity and mortality from measles.

The community-based morbidity trials assessing impact on diarrhea and acute respiratory infection, however, have given conflicting results. Two trials reported increased incidence of mild acute respiratory infection and diarrhea in treated children. Two hospital-based studies have also shown no therapeutic benefit in children with pneumonia or diarrhea. However, two other studies have shown that vitamin A supplementation impacted significantly on reducing the severity of disease.

At this meeting, reports of field trials from Sudan (59) and Bangladesh (60) indicate that vitamin A prophylaxis was associated with increased morbidity (acute respiratory infection and acute respiratory infection/diarrheal diseases, respectively). A hospital-based trial in Tanzania also demonstrated no effect of vitamin A therapy in children with pneumonia (56). On the other hand, a study in India found a 30% reduction in persistent diarrhea and another reported a 10% reduction in overall child morbidity (acute respiratory infection and diarrheal diseases) (58).

The lack of a beneficial effect and the finding of a possible adverse effect of vitamin A prophylaxis does not imply that vitamin A has no role in reducing morbidity. There is sufficient evidence to indicate that vitamin A is important in terms of preventing severe disease, particularly that related to diarrhea and, ultimately, death.

Many countries have a policy of treating pneumonia with vitamin A. Should these policies be changed given the negative findings of the published and unpublished studies? The idea is that vitamin A should still be used in patients with pneumonia, not as a cure for pneumonia but to prevent possible depletion

of stores that may occur with infections, particularly repeated infections. The study from Bangladesh that identified acute respiratory infection as being an important risk factor for inadequate vitamin A status supports this view (80). In addition, vitamin A will benefit children with pneumonia, because they are frequently undernourished and have concomitant diarrhea.

The other concern raised in the meeting is whether additional vitamin A efficacy trials in children presenting with acute respiratory infection should be carried out, because such trials are logistically difficult and expensive. It is the opinion of some individuals that such trials will not be beneficial unless they focus on respiratory syncytial virus pneumonia. Why respiratory syncytial virus? Like measles, it is a paromyxovirus, which has a predilection to damage the respiratory epithelium, thus, if vitamin A is beneficial in treating pneumonia then it should also be beneficial in treating respiratory syncytial virus. Two such trials in developing countries are currently under way, hopefully, these studies will resolve some of the problems.

#### *Parasitic infections and vitamin A*

Parasitic infestations are a major cause of childhood morbidity. A policy of regular mass deworming has been advocated and is practiced in many countries. Investigators from a study in Zanzibar reported that, despite significant parasitic infections in children, vitamin A status was good (90). The mean vitamin A level was about 30 µg/dL and none of the children was vitamin A deficient.

#### **Vitamin A Status and Growth**

*Low-birth-weight infants* It has been generally accepted that the vitamin A status of an infant is related to that of the mother. Three papers examined the association between maternal and infant retinol status (77, 78, 103).

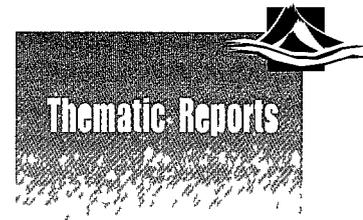
The reasons for, and the consequences of, inadequate vitamin A status

in both the mother and infant during the perinatal period are not fully understood. Research in this field should be encouraged, particularly in areas with high perinatal mortality rates and in situations where maternal and neonatal sepsis is prevalent.

#### **Vitamin A and Micronutrients**

*Vitamin A and anemia* The interaction between vitamin A and anemia has been well documented. Anemia is a recognized consequence of VAD and improved hemoglobin status has resulted from vitamin A therapy. Four studies were presented at the conference. A study from Dhaka in adolescent girls confirmed that a significant correlation existed between vitamin A and hemoglobin (41). An Indonesian study evaluated three different regimens of vitamin A/iron combinations (compared with placebo) in anemic high school girls. A weekly iron (60 mg) and vitamin A (20,000 IU) regimen was most effective in improving hemoglobin but not iron stores (39). A study from the Marshall Islands reported no effect on hemoglobin status after treatment with vitamin A, but this may have been due to the small sample size (38). The last study investigated the influence of iron supplementation on the health of infants in Pakistan by measuring markers of infection and retinol intake (40). Data suggested that iron supplementation may be deleterious in infants exposed to infections but that these effects may be reduced by improving vitamin A status.

*Vitamin A and iodine deficiency disorders* Limited data exist on the association between vitamin A and iodine deficiency disorders. One paper from Iran reported that serum retinol but not β-carotene was significantly lower in iodine-deficient women compared to nondeficient women (42). The study concluded that carotene conversion to vitamin A may be disturbed in iodine-deficient persons. The interaction between iodine and vitamin A needs further investigation, particularly in areas where iodine deficiency disorders are prevalent.





### ***Risk Factors and Reasons for VAD***

Assessment of risk factors in any disease is important, because it helps to define appropriate intervention strategies. Descriptive studies on population-based assessments of vitamin A status done in a number of countries have highlighted poor socioeconomic status to be a significant risk factor for vitamin A insufficiency. This once again emphasizes that strategies directed to improving vitamin A status should focus not only on medical interventions but also on specific risk factors that are important when it comes to targeted interventions.

Two analytical studies presented at this meeting provided interesting detailed information about risk factors for VAD. A study reported from Nepal is the first case-control study that has defined specific risk factors for night blindness in pregnancy (79). Further studies in other areas need to be encouraged. In another study, it was found that vitamin A supplementation at the time of immunization did not improve status in a subset of children who had frequent respiratory tract infections (80). This study has emphasized the importance of frequent infections as a cause of VAD.

A decrease in serum vitamin A is noted in a wide variety of infective and febrile conditions and is probably a manifestation of the acute-phase response. Reduced liver stores have also been reported to follow infections.

Two studies, one clinical and one experimental, addressed this subject. A study from Peru found that acute diarrhea is accompanied by a reduction in serum retinol and significant excretion of retinol-RBP in the urine that is probably associated with the acute-phase reaction (81). The significance of the study is that depletion of vitamin A stores and progression to persistent diarrhea may be a consequence.

The experimental study suggested that VAD is the result of reduced hepatic synthesis and secretion of retinol-RBP and that plasma vitamin A is a poor

indicator of vitamin A status in infection (82).

Retinol homeostasis, particularly during infections, is a complex phenomenon that is not entirely understood. These two papers have provided some information. However, further studies designed to unravel this complex problem are needed.

In conclusion, the papers presented at this conference have highlighted new and significant findings and have clarified some issues relating to the biological significance of vitamin A. Other papers have raised a number of questions that require further investigation. It is hoped that the answers to these questions will be presented at the next IVACG meeting.

### **APPROPRIATE INTERVENTIONS**

Ms Victoria Sheffield (111) summarized the knowledge gained about appropriate VAD interventions.

The evolution of the battle to control VAD has progressed to the point where knowledge and technology have allowed for implementation of effective programs. Projects have been implemented with various degrees of success and failure. Now there is a need to refine the approaches, share ideas, and address VAD with the same vigor directed to treatment for xerophthalmia. Dr Horwitz recommended that the government, the private sector, and NGOs work more in collaboration and share their knowledge and technology (18). Sir George Alleyne (3) said that vitamin A people need to take a "bungee jump" forward. This can be done only through multisectoral approaches and direct collaboration with sectors other than the traditional health and nutrition communities.

In the presentation on the role of NGOs, there was a reminder that NGOs should continue to serve as advocates for change and keep the control of VAD a priority in endemic countries.

The review of USAID's involvement in VAD control on the first day of the

meeting reminded us that VAD control should be a policy wherever programs addressing child mortality are being implemented (37)

During the discussion of “Sustainability in Vitamin A Programs,” capsule distribution, fortification, and food availability interventions were seen as complementary and all three may still be needed even as countries reduce their rates of VAD (87, 88)

### ***Vitamin A Capsule Distribution***

Vitamin A capsule distribution should be considered an appropriate intervention where xerophthalmia is a problem or in pockets where at-risk populations have no access to other interventions. Two papers from Bangladesh showed that capsule distribution programs can be efficiently implemented in conjunction with immunization programs linking distribution to the 9-month measles immunization and the 18-month DPT contact (91, 92)

### ***Food Fortification***

A number of papers discussed fortification of specific foods, especially sugar, and reviewed the history and lessons learned in development of this intervention. Dr. Purvis advised that the “establishment of food intake and nutritional need are necessary to provide fortification guidance, vehicle, quantity, and extent of fortification (44)”

This paper, along with the review of the MSG fortification process (46) and presentations reviewing lessons learned in sugar fortification in Central America (45, 48, 51) enforce the need for a multisectoral or interdisciplinary approach from the earliest stage of the development process. The presenters specified the following:

- 1 Political commitment and policy legislation are critical to ensure financial sustainability and economic viability

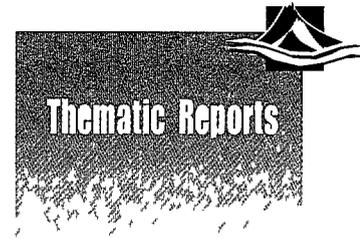
- 2 Food producers should be the lead partner in any food fortification effort
- 3 Profitability for the food producers is the major consideration in engaging their support for any fortification effort
- 4 Sustainability is more likely to be achieved when countries design and implement fortification programs when they are economically able to afford them
- 5 Ongoing monitoring and evaluation at the mill, distribution, and household sites are critical factors in quality control of fortification programs
- 6 Fortification programs should explore cost recovery mechanisms that include consumer cost, government subsidies and tax incentives, and bank loans

Packaging is a factor in food fortification. Presenters noted that the combination of high environmental temperature and humidity is the main cause of deterioration of retinol in fortified sugar. Therefore, packaging should be as airtight as possible. Higher-quality packaging will come with economic development, but for the moment, the amount of retinol remaining in sugar, under actual conditions, is sufficient to generate a biological impact in human populations. Presenters also recommended that investigation of consumer preferences for package size should be conducted to determine appropriate packaging to satisfy consumer demand for sugar.

### ***Dietary Interventions***

The experiences of HKI in Bangladesh have shown that the type of garden is a determinant for intake (61). Their studies have shown the following:

- 1 Greater choice of vitamin A foods is likely to increase consumption of vegetables
- 2 The mixed type of gardens growing diverse vitamin A-rich foods versus





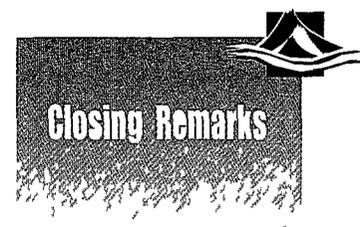
**D**r Horwitz (112) stated in his closing remarks that the XVII IVACG Meeting has shown the diversity of ideas explored, the different subjects examined, the richness of studies, the suggestive conclusions, and the significance of the knowledge unraveled. It is rewarding that the majority of the presentations came from developing countries. The participants were reminded of the long task ahead to reach the goal of virtual elimination of VAD, because by current estimates, 250 million children are at risk. Dr Horwitz said one of the major obstacles is the lack of coordination among and between different sectors involved in the VAD prevention and control program. Coordination is also needed among the international organizations. According to Dr Horwitz, solutions are tailored for specific obstacles and can always be implemented if resources are available.

As examples of obstacles and solutions for reaching the goal, he cited the experiences of India and Tanzania. In India, when a National Nutrition Policy and a National Plan of Action in Nutrition were formulated, the virtual elimination of VAD was included (20). The implementation of the policy and plan of action required a comprehensive multisectoral approach. Major obstacles included the lack of an appropriate coordinating body, low priority given to nutrition, lack of political commitment, lack of trained manpower, and inadequate financial resources. Solutions have been found for most of these obstacles,

particularly for prevention and control of VAD, including supplementation, food fortification, and dietary diversification.

The Tanzanian experience in combating VAD was developed through two 5-year plans between 1985 and 1995 (23). Major constraints in the first plan were inadequate technical expertise, lack of awareness among policy makers and communities, and lack of problem assessment and analytical tools. Solutions have been applied to all of them, with intensive use of the IEC system. In the second plan, the major obstacles involve inadequate financial and human resources, insufficient communication infrastructure, and ineffective management at different levels. Some of these constraints require long-range solutions, especially investment of financial resources in effective program management. This exercise of drawing on the experiences of different countries should be encouraged at the next meeting.

Finally, Dr Horwitz referred to Dr Jonas Salk, the discoverer of the first polio vaccine, who believed that one *feels* things before one *knows* what one feels. This way of thinking seems to apply to all who are devoted to prevention of VAD. The scientific answers may not all be there, but there is the *intense feeling* of the tragic consequences of the lack of them in children, namely blindness and death. This is the reason why the condition should be eliminated in the world without waiting for all the scientific knowledge related to vitamin A.





*NOTE At the close of the XVII IVACG Meeting, the following recommendations were prepared by the meeting rapporteurs and the IVACG Steering Committee for the purpose of clarifying data and discussion that might impact on policy*

Some countries have effectively eliminated xerophthalmia as a public health problem, but many still have significant VAD with untoward impact on childhood morbidity and mortality

There is likely to be a continuing need for vitamin A supplements even when other sustainable programs have replaced the need for wide spread supplementation

Immunization programs provide an excellent opportunity for delivering vitamin A supplements. Data presented at this meeting provided reassurance that vitamin A supplements given in conjunction with measles vaccine to 9-months old children will not interfere with measles seroconversion

There is a growing body of evidence for a relationship between vitamin A status and HIV/AIDS clinical status

- Whether this has implications for vitamin A therapy remains to be determined

• Night blindness is easier to detect in adults than in children. In communities where night blindness is prevalent in women during pregnancy and lactation, it should be considered an indicator of potential VAD

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In assessments of vitamin A status of a population by means of serum retinol, the presence of infection among those sampled needs to be taken into account when interpreting the results

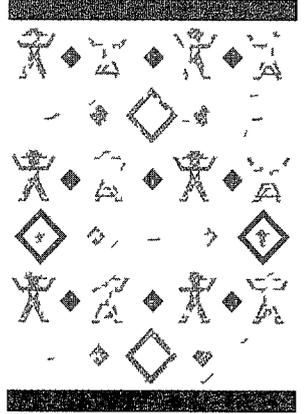
VAD can exacerbate anemia. In treating anemia, one should be sure that the population is not also vitamin A deficient

More reliable data on  $\beta$ -carotene content of foods is needed. To interpret these data in terms of provitamin A activity, the bioavailability of these foods needs to be known. Carotenoid in some foods, such as red palm oil, mango, papaya, and yellow sweet potatoes, is particularly bioavailable. The method by which foods are harvested, stored, and prepared will affect their provitamin A content and bioavailability, and this needs to be considered when food composition tables are constructed

Finally, each country should formulate programs that contain a mixture of the three primary approaches for increasing vitamin A intake: supplementation, fortification, and dietary diversification. The relative importance of each component should be suited to the particular local conditions and resources in each country. Integration into ongoing health programs is likely to facilitate and sustain the impact of these activities



# References



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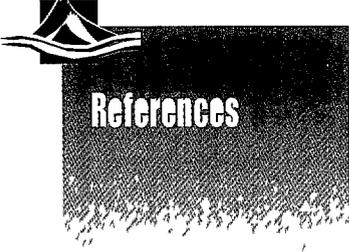
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NOTE Names given in italics are those people who spoke at the meeting or were responsible for poster presentations References are to presentations given during the meeting, abstracts of most of these presentations are included in this report (and can be found on the page given in italics at the end of the reference)

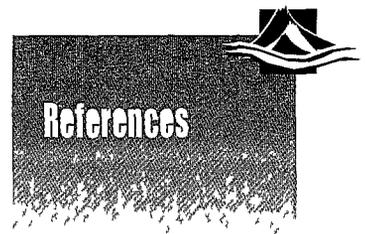


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- 4 *Ing Marco Tulio Sosa Ramirez*, Opening address
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- 8 *Interiano E*, Prevention and control of vitamin A deficiency in El Salvador
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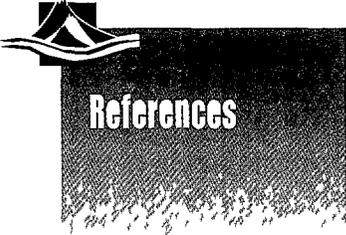


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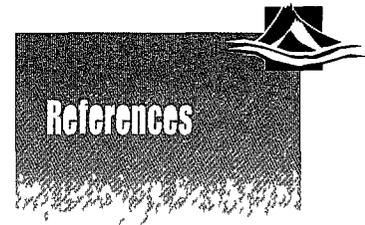
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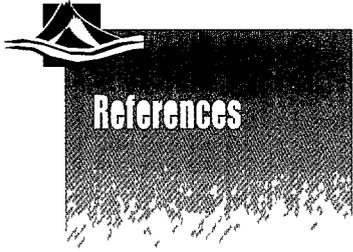


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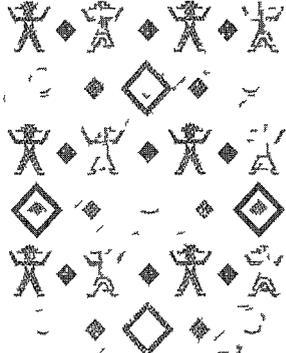


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# Abstracts



**Obstacles and solutions for reaching the goal of virtual elimination of Vitamin A Deficiency by 2000, Indian experience Vinodini Reddy**

Vitamin A Deficiency (VAD) has long been recognized as a major public health problem in India, severe forms of deficiency leading to blindness in children. Large scale intervention measures have been initiated to reduce prevalence of the deficiency. These include vitamin A supplementation, fortification of foods and dietary diversification. Although recent surveys show a declining trend in the prevalence of xerophthalmia, virtual elimination of VAD by 2000 is a formidable challenge. The national vitamin A supplementation program has been in operation for more than 2 decades although it was envisaged as a short term measure to reduce blindness in children. Evaluation studies showed poor coverage due to inadequate supplies, poor coordination between various health functionaries and lack of supervision. Appropriate measures were taken to overcome them. In the revised strategy, delivery of vitamin A is linked with immunization to improve the coverage. Although vitamin A supplementation is a simple and effective intervention, it is only a temporary measure to control the problem. The root cause of VAD is dietary inadequacy and it is increasingly recognized that such medicinal supplements will not solve the problem. In recent years, there has been a change in the policy with greater emphasis on long term food based interventions. It is also realized that malnutrition is a social and not a medical problem, and measures outside health sector are also necessary to improve nutrition. This realization has led to the formulation of a National Nutrition Policy in 1993 with emphasis on a comprehensive multi sectoral strategy to achieve the nutrition goals. A National Plan of Action has been formulated recently involving various sectors including health, agriculture, food, education, women and child development for implementation of the nutrition programs including specific measures to combat VAD. The challenge lies in developing mechanisms of coordination for converging services at the community level.

**TANZANIA'S EXPERIENCE IN COMBATING VITAMIN A DEFICIENCY: A CASE HISTORY** G. D. Ndossi, TFNC  
Ocean Road No. 22 Dar es Salaam Tanzania

Vitamin A deficiency (VAD) is a problem of public health significance in various parts of Tanzania. The Tanzania Food and Nutrition Centre (TFNC) has estimated that VAD and xerophthalmia affects about 1.4 million people or 6.1% of an estimated population of 22.3 million people in 1988. Concerted efforts to eliminate the problem started in 1981 and by 1985 sufficient evidence had been obtained to justify the initiation of a national programme. Hence the first five year programme was started in 1985. The short-term objective of this programme was to make available vitamin A capsules (VAC) to children at high risk of developing xerophthalmia. The long-term objective was to promote regular and adequate dietary intake of vitamin A among young children. The major achievements between 1985 and 1990 were the following: The identification of a lead agency (TFNC) with technical and managerial capacity; Building consensus across sectors through advocacy; Development of a national plan of action; The formation of a multisectoral policy and steering body for the implementation of the programme. At the end of the first programme it became clear that it was necessary to continue and strengthen the efforts which had been ongoing. Thus the second five year programme was formulated in 1990 and will end in 1995. Achievements made during the second programme include the following: Distributed VAC to all dispensaries and rural health centres; Initiated pilot scale production of vitamin A rich fruits and vegetables at community level; Conducted nation-wide workshops to health personnel on the diagnosis and management of VAD; Conducted various operations research related to the control and prevention of VAD. The present paper will provide a case history of Tanzania's experience in combating VAD over the last 10 years.

**NATIONAL VITAMIN A DEFICIENCY CONTROL PROGRAMME IN GHANA** R. Agble and E. Amoah, Ministry of Health Nutrition Unit, P.O. Box M78 Accra, P. Arthur Health Research Unit, Ministry of Health Kintampo and M. Armar Klemesu Noguchi Memorial Institute for Medical Research Accra

Various studies have confirmed a serious vitamin A deficiency disorder in the Northern sector of the country and a potential problem in the South. This has prompted the Ministry of Health to formulate a national programme for the control of vitamin A deficiency in collaboration with relevant ministries.

The four components of the programme are:

- 1) Formulation of policy on Vitamin A for the treatment of measles
- 2) Periodic supplementation in the Northern sector (Upper East, Upper West, Northern) where Vitamin A deficiency is severest and largest, using different strategies
- 3) Exploring potential dietary interventions
- 4) Describing the vitamin A situation in the Southern part of the country

Progress that has been made to implement the national programme so far include adoption of policy position by the Ministry of Health, reaching national consensus among policy makers and national and regional implementers, and the formation of multisectoral coordinating group.

Obstacles that may prevent the achievement of the global goal of eliminating vitamin A deficiency by year 2000 include:

- 1) Inadequate advocacy both at the international and national levels
- 2) Central control and bureaucracy within the Ministry of Health
- 3) Variable picture of Vitamin A Deficiency problem which will involve different strategies in various parts of the country and involve different sectors

**INTERACTION OF MICRONUTRIENTS TO BUILD PRE PREGNANCY IRON RESERVES IN ADOLESCENT GIRLS THE ROLE OF VITAMIN A** Angeles I Schultink W Sastroamidjojo S Gross R Karyadi D SEAMEO Nutrition Center Jakarta Indonesia and GTZ Eschborn Germany

Anemia among adolescent girls may be a determinant of anemia during pregnancy. Different types of combined supplementation were investigated in order to improve iron status among adolescent girls. Subjects were 281 high school girls aged 14-17 y of which 20.9% were anemic. The study was conducted in a randomized, double-blind manner with subjects taking either a placebo or a micronutrient-containing tablet on each of the seven days of the week.

Table. Dosages and schedules of ingestion

	iron(mg)	vit A(IU)	vit C (mg)	folate ( $\mu$ g)	A/Fe
Group 1	60 <sup>1</sup>	2500	60	250	42
Group 2	60 <sup>1</sup>	20000	60	500	333
Group 3	120 <sup>1</sup>	20000	60	500	166
Group 4	0 <sup>1</sup>	0	0	0	0

1 Daily supplementation on school days

2 Supplementation on a once weekly basis with a placebo on remaining school days

The important variables were the dose of iron, the periodicity of the dosing, and the vitamin A/iron ratio. The hypothesis of interest here is whether or not an independent vitamin A dosage effect could be paralleled out with respect to changes in hemoglobin and ferritin after 8 wks of intervention.

Prevalence of low serum retinol (<0.70  $\mu$ mol/L) varied between 20.2% (group 1) and 35.4% (group 3) (p=0.04). At finish, the mean retinol concentration had increased with 0.25, 0.27, and 0.26  $\mu$ mol/L in groups 1, 2, 3 respectively, these increments being larger (p<0.001) than that of 0.08  $\mu$ mol/L in group 4. Hemoglobin increased significantly in groups 1, 2, 3 (p<0.001) with changes varying between 6 g/L (group 1) and 5 g/L (group 3). Ferritin increased with 26  $\mu$ g/L in group 1 (p<0.001) and with 9  $\mu$ g/L in groups 2 and 3 (p<0.001). Hemoglobin and ferritin decreased slightly in group 4, and these changes differed significantly from increments in groups 1, 2, 3 (p<0.001). Ferritin increments in group 1 were also larger than in groups 2 and 3 (p<0.001). A combined iron-vitamin A supplement (60mg, 20000 IU) was most effective in increasing Hb, but less effective in increasing iron stores than daily iron-vitamin A supplements. A change in iron-vitamin A ratio when supplemented on a weekly basis did not have any effect on iron status.

**A COMPARISON OF SERUM RETINOL LEVELS WITH HEMOGLOBIN CONCENTRATIONS BEFORE AND AFTER VITAMIN A CAPSULE DISTRIBUTION IN ONE TO FIVE YEAR OLD CHILDREN IN THE REPUBLIC OF THE MARSHALL ISLANDS** NA Palafox M Gamble C Kojhede J Gittlesohn K Briand B Blaner J Langidrik John Burns School of Medicine University of Hawaii Hawaii USA Columbia University Institute of Human Nutrition Columbia NY USA Johns Hopkins School of Hygiene and Public Health Division of Human Nutrition Baltimore MD USA Ministry of Health and Environment Republic of the Marshall Islands (RMI) Majuro RMI

Health Data from the Republic of the Marshall Islands suggests that the children of the Marshall Islands have a rising burden of iron deficiency anemia and Vitamin A deficiency (VAD). In 1987 there was 3% anemia whereas in 1991 and 1995 33% and 39% respectively of children were anemic. Population studies have found positive correlations between serum retinol (ROH) and biochemical indicators of iron status in childhood anemia. Low serum hemoglobin (Hgb) had a 75% sensitivity and 40% specificity in predicting VAD. Animal studies suggest that the efficiency of apparent iron absorption was increased by intake of vitamin A when iron stores were adequate. The objective of this study was to: 1) characterize the relationship of low Hgb and low ROH in various age strata in Marshallese children ages 1-5; 2) measure the difference of ROH and Hgb one month after the initial Vitamin A capsule distribution; 3) determine possible relationships between Vitamin A supplementation and Hgb levels. Methods: Hgb and ROH measurements were obtained from 800 Marshallese children who were randomly selected from four designated geographic strata. The distribution of children with Hgb < 11 mcg/dl was compared to distributions of ROH. Subsequently a random sample of 200 children from two atolls had Hgb, ROH, retinol, serum iron and ferritin levels drawn one month post Vitamin A capsule distribution. The results were analyzed to determine if there were significant changes in the distribution and prevalence of Hgb < 11 g/dl and ROH. Ferritin and serum iron were utilized to get an index of the iron status of children in the sample population. Findings: The beta coefficient (ROH as the dependent and Hgb as the independent variable) was 1.4. The analysis and data of the blood testing done one month post Vitamin A capsule distribution is in process. Conclusion: There is a high correlation between children with Hgb levels less than 11 mcg/dl and ROH levels < 20mcg/dl.

Acknowledgements: UNICEF Suva Fiji; Ferguson Foundation Kona Hawaii; Department of Family Practice University of Hawaii.

**VITAMIN A AND BETA - CAROTENE STATUS IN IODINE DEFICIENCY** M Kimiagar and A Vahidi - nia National Nutrition and Food Technology Research Institute P O Box 19395 - 4741 Tehran I R Iran

The relationship between vitamin A status and iodine deficiency has been reported in the past but the proof is scanty. Our previous observations in endemic areas bore evidence to the existence of lower vitamin A levels in goitrous euthyroid as well as hypothyroid subjects. The need was felt therefore, to distinctly examine and compare iodine-deficient versus iodine-sufficient groups as to their vitamin A status. For this reason 55 women 20 years of age and over in Vardij, an iodine deficient (ID) village (water iodine 1.7  $\mu$ g per liter, urinary iodine excretion 43  $\mu$ g/g creatinine) and 37 women in Kolein an iodine sufficient (IS) village (water iodine 10  $\mu$ g per liter, urinary iodine excretion 197  $\mu$ g/g creatinine) were chosen. Serum thyroidal hormones, retinol and beta-carotene were measured. No subject was either hypo- or hyper-thyroid. Serum retinol was reduced with goiter enlargement while serum beta-carotene was elevated (p<0.001). Marginal vitamin A deficiencies were more prevalent in ID subjects. In general, thyroxine, FT<sub>4</sub> I and serum retinol were positively correlated and simultaneously reduced in ID subjects. On the other hand, beta-carotene was elevated with decreases in T<sub>4</sub>, FT<sub>4</sub> I and T<sub>3</sub> levels. Beta-carotene to retinol ratio was 2.65 in IS and 3.59 in ID subjects (p<0.01). Based on these data it is concluded that serum retinol reduction is associated with the thyroid enlargement. It is also suggested that not only in hypothyroidism but also in iodine deficient euthyroid subjects the beta-carotene to retinol conversion is disturbed. This leads to serum retinol diminution which in turn might aggravate iodine deficiency.

**THE BIOAVAILABILITY OF DIETARY CAROTENOIDS** James Allen Olson  
Biochemistry & Biophysics Iowa State University Ames, IA 50011 USA

Of the >600 carotenoids found in nature the bioconversion of approximately 50 dietary carotenoids into vitamin A has repeatedly been demonstrated. Proformed vitamin A, usually ingested in the presence of fat, is well absorbed from the intestinal tract, transported in chylomicra to the liver and other organs and efficiently stored in vitamin A-containing globules of stellate and parenchymal cells of the liver. The absorption efficiency of vitamin A is only slightly affected by the amount ingested. The utilization of dietary carotenoids is by no means such a straightforward process. First of all many carotenoids are bound tightly in the essentially fat free matrix of vegetables, from which they are released with difficulty. Cooking while denaturing parts of the matrix, also induces oxidative inactivation of carotenoids. Similarly carotenoids dissolved in highly unsaturated oils that do not contain antioxidants are rapidly inactivated. Many elements of the vegetable matrix that are not hydrolyzed by digestive enzymes make up the fiber component of the diet. Thus cooking vegetables although generally enhancing the bioavailability of carotenoids do not always do so. Grinding or pureeing foods usually increases carotenoid bioavailability. Some fat is necessary for carotenoid utilization both to stimulate bile flow as well as to solubilize the hydrophobic carotenoids in lipid aggregates. The processes of micellization and intestinal absorption show rigorous requirements for bile acids. Thus lipid malabsorption syndromes markedly lower carotenoid utilization. Severe parasitic infection might also play an adverse role. Carotenoids seem to be better absorbed from fruits such as mangoes and papayas, and are much better utilized when present in oils such as red palm oil. Nonetheless as the amount of carotenoid ingested increases its intestinal absorption efficiency decreases. Thus a variety of factors influence the nutritional value of provitamin A carotenoids relative to vitamin A. The WHO/FAO nutritional ratio defined in 1967 and in large part accepted by others is that 6  $\mu\text{g}$  all trans  $\beta$  carotene in food = 1  $\mu\text{g}$  all trans retinol. Isomeric forms of  $\beta$  carotene and other provitamin A carotenoids are  $\leq 50\%$  as active. The nutritional ratio for a given meal or for a given diet, of course can be much higher or much lower depending on the factors cited earlier. The lowest ratio that has been observed experimentally is 2  $\mu\text{g}$   $\beta$  carotene = 1  $\mu\text{g}$  retinol which is probably a function of the relative intestinal absorption efficiencies. Because of the public health significance of vegetables as sources of provitamin A carotenoids new ways of enhancing carotenoid bioavailability in vegetables merit careful further attention. (Supported by NIH DK 39733 USDA CRG 94-37200 0490 and USDA/ISU/CDFIN 94-34115 0269)

## Vitamin A Fortification of Foods

## Oral Presentations

**FORTIFICATION ISSUES AND CONSIDERATIONS** George A. Purvis, PhD  
OMNI Fortification Consultant Michigan State U Fremont Michigan USA 49412

Food fortification is a preferred method for delivery of micronutrients for a number of technical and practical reasons. Advantages are apparent when compared to other delivery methods: supplementation and parenteral administration. Foods or food ingredients consumed in significant and consistent quantities by the target population are available as fortification vehicles. Fortificants with food grade quality are available for most micronutrients which are compatible with food systems and bioavailable in the foods consumed. Flexibility can be accomplished by adjustment of nutrient concentration to fit food intake and nutritional need. Fortification can be focused to deliver nutrients to target populations. Mixing with food or food ingredients provides insurance of safety from overdose. Costs are lower than other delivery systems and can usually be incorporated as a part of the food cost with insignificant price increase.

Examples are available which demonstrate fortification with a variety of nutrients and foods. Wheat flour has been fortified for decades with iron and selected vitamins. Prepared cereal can be fortified with an entire spectrum of micronutrients. Milk and milk based food fortification with fat soluble vitamins is compatible.

Practical constraints do exist but most can be addressed with available technology: quality issues (primarily flavor and color changes), interactions with food components and formation of complex compounds. Program cost is a constraint and must be evaluated relative to benefit to allow realistic policy action. Establishment of food intake and nutritional need are necessary to provide fortification guidance: vehicle, quantity and extent of fortification.

A program for micronutrient fortification of foods involves an interdisciplinary approach to bring together all available resources: administrative, scientific, technical, regulatory and policy to apply available experience, knowledge and influence to identify and overcome specific nutritional deficiencies.

**KEY ISSUES FOR IMPLEMENTING A PROGRAM OF SUGAR FORTIFICATION WITH VITAMIN A: THE CENTRAL AMERICAN EXPERIENCE** Guillermo Arroyave  
San Diego, California (USA)

Because vitamin A deficiency in the Central American region was extensive, affecting large sectors of the population, food fortification was considered a very appropriate intervention. White sugar met the criteria as food vehicle. Due to widespread consumption, its ample population coverage ensured that even the most vulnerable groups would be benefitted. Through seven years of laboratory and pilot research, the technology was developed at INCAP to fortify sugar with a special water-miscible vitamin A preparation, a product known as 250-CWS, first obtained from Hoffman-LaRoche. Once the technology was available, a program had to be developed: key elements were built-in systems of quality control and monitoring to ensure that an adequately fortified sugar reached the target consumers, and an evaluation component to assess the nutritional impact of the intervention. The implementation of sugar fortification as a national program required full consensus and cooperation between the government and the sugar manufacturers. With the technical assistance of INCAP, they were the main parties in elaborating the master program plan including cost analysis and the proposed legal/regulatory instruments. The laws that were approved by Guatemala and other Central American countries made sugar fortification with vitamin A compulsory and defined the basic and operational norms for the production, marketing and distribution of the product. A before-and-after two-year evaluation carried out in Guatemala using dietary and biochemical indicators, demonstrated the remarkable effectiveness of this nutritional intervention.

LESSONS LEARNED IN THE DEVELOPMENT OF THE MSG VITAMIN A FORTIFICATION PROJECT Robert L. Tilden Benny Kodyat and Muhulal University of Minnesota Medical School Duluth Clinic Duluth Minnesota, Nutrition Unit, Ministry of Health, Jakarta Indonesia and Center for Research and Development of Nutrition, Bogor Indonesia

The MSG vitamin A fortification project in Indonesia was undertaken in several stages Intensive research for 1) potential food commodities as candidate fortification vehicles 2) project planning 3) product and package development took place prior to the implementation of the first community intervention pilot project Pilot project development was complicated by opposition from producers the consumers union, and units within the Ministry of Health as well as by low levels of financial assistance Despite these obstacles the pilot project was successful and substantial impact was achieved on the health of pre school children. However later on in the project during the pre national implementation phase when opposition had diminished and adequate funds were available the project faltered and was ultimately halted

We review the successes and failures of the project starting with the pioneering work done during the Nutritional Blindness National Prevalence Survey in 1976-78 continuing through the pilot project development period in 81-84 into the implementation of the pilot project in 84-86 and finishing with the pre national program in 1990 Successful program outcomes including food commodity identification early product development progress of political momentum for project approval and development of a productive working relationship with one of the MSG producers are reviewed The political and technical factors contributing to failure of the project to develop into a national program are also discussed In the future it is hoped that countries interested in developing vitamin A fortification programs understand that adequate time and productive partnerships with business and political will are all necessary for the development of a successful fortification project, and that potential donors appreciate the need to tailor their technical support to the projects cultural and administrative environment.

## Oral Presentations

## Experiences with Vitamin A Fortification of Foods

SUGAR FORTIFICATION A CHALLENGE OF VITAMIN A DEFICIENCY IN HONDURAS R Hernández and D Chunchilla Ministry of Health and PAHO/INCAP Representative Honduras Central America

One of the most important interventions carried out in Honduras in order to reduce the prevalence of the lack of vitamin A is the fortification of sugar

According to the Survey of Food Consumption, 1987 (SFC/87) 73% of the families consumed less of the half of the nutritional recommendation of Vitamin A. Studies and experiences in Central America, point out that sugar is the ideal vehicle for the fortification of Vitamin A Moreover the SFC/87 estimated a daily consumption of sugar of 40g per capita This information served as the basis for the approval of the law for the Fortification of Sugar with Vitamin A in 1977

The Ministry of Health (MOH) showed that from 1977 to 1983 approximately 50% of the sugar produced was fortified In 1983 the process gets in transition, becomes stagnant and is occasionally interrupted. In 1987 the MOH began the systematic analysis of sugar produced and sold at the national level noting low or nonexistent levels of Vitamin A from the samples taken from sugar mills and markets In 1990 91 only 28.8% was fortified and of this amount 10% contained the required retinol levels

The 1992 evaluation identified the most important critical points of the fortification process As an answer to the problems identified the MOH provided a special premixer for Vitamin A and sugar and the methods for fortification were standardized operation manuals for the preparation of premix and fortified sugar were issued and various workers were trained in such methods In 1993 a dialogue between the government and the sugar industrals began, with the main purpose of setting goals for increasing the amount of fortified sugar and improving the quality of the fortification.

Monitoring of the process was established at three levels 1) Information from the quantity of fortified sugar at the end of the sugar cane harvest and projections for the next sugar cane harvest Reports show that during 1993 and 1994 the amount of fortified sugar has been approximately 50% of the sugar for internal consumption 2) Chemical analysis of samples of fortified sugar taken from sugar mills markets and homes The evaluation of 1993 showed that 75% of the sugar in the mills was fortified In 1994 94% of sugar for human consumption was fortified and 55% of the samples had adequate vitamin A levels 3) Evaluation of the biological impact by determination of Retinol in blood in the population. No updated data is currently available A seroprevalence survey will be carried out during the second semester of 1995

Honduras faces the challenge of achieve 100% fortification while search for behaviour changes in the population toward an adequate diet in order to avoid Vitamin A deficiencies in the more vulnerable populations

RETINOL STABILITY OF FORTIFIED SUGAR IN GUATEMALA

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In prior studies it was determined that 85-90% of the initial retinol content remained in sugar after 9 months of storage However this evaluation was not carried out under different weather conditions neither using the typical containers used to deliver sugar to the final consumers The main objective of this study was to determine the stability of retinol in fortified sugar at the household level and under typical climatic conditions in Guatemala

Sugar was fortified at 30 µg retinol/g and packed in 1.0 and 12.5 pounds transparent polyethylene bags protected or not from light exposure Sugar was stored in four Guatemalan cities simulating kitchen conditions during one year Retinol content was determined spectrophotometrically every month

As expected retinol stability was lower in humid and warm locations Apparently container size and type did not affect the stability of retinol except in the warmest and wettest place where sugar itself stored in 1 pound containers gained so much water that turned unacceptable to consumers starting at the 9th month Retinol levels after 6 months of storage were 62 to 77% of its initial content (half life values from 9 to 18 months) coinciding with reported retinol stability for fortified beverages without air exposition Using the current level of fortification (15 µg/g) the usual sugar consumption and the retinol loss rate it was calculated that in all places persons of the groups at the highest risk of suffering vitamin A deficiency are fulfilling almost all their vitamin A requirements and approximately half of the RDA values through fortified sugar These results confirm the nutritional effectiveness of this intervention

#### HOUSEHOLD LEVEL MONITORING OF FORTIFICATION PROGRAMS

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Guatemala is one of the pioneers in micronutrient food fortification. Salt has been fortified with iodine for over 20 years while sugar has been fortified with vitamin A by all of the major sugar producers since the late 1980s. Formal legislation exists which sets limits of acceptable levels of fortification for both of these micronutrients. Monitoring of the fortification process is generally performed by the producers. To better understand how existing fortification efforts were reaching local population, the IEF collected 66 samples of both salt and sugar (WHO/EPI 30 clusters sampling approach) from households in 27 communities in the Department of Alta Verapaz, Guatemala, where it conducts vitamin A supplementation, nutrition education, home gardens and child survival activities. Salt samples were analyzed using the semi-quantitative MBI field kit method. The legally mandated level of iodine fortification is 30-100ppm. The following results were obtained:

≤ 15ppm	≤ 30ppm	≤ 40ppm	≤ 50ppm
62% (n=41)	85% (n=56)	89% (n=59)	100% (n=66)

Note that fifty percent of the under 15 ppm samples were less than or equal to 7 ppm and only 15% of samples fell within the legal range.

Sugar samples were analyzed using a quantitative spectrophotometric method in order to compare levels of retinol in the household samples with the legally mandated level of 5 to 20µg/g. A total of 60% of the samples fell within the legally mandated range. The results were as follows:

≤ 5 µg/g	≤ 10µg/g	≤ 15µg/g	≤ 20µg/g	≤ 25µg/g	≤ 30µg/g	≤ 35µg/g
29% (n=19)	62% (n=41)	85% (n=59)	89% (n=59)	95% (n=63)	98% (n=65)	100% (n=66)

These data show that local efforts to monitor sugar and salt fortification at the household level are essential to ensure adequate and consistent micronutrient fortification.

A SCHOOL DISTRIBUTED COOKIE IS AN EXCELLENT SOURCE OF VITAMIN A IN GUATEMALA. M. Guamuch, O. Dary, and L. De León. Institute of Nutrition of Central America and Panama, Guatemala City, Guatemala.

INCAP formulated a highly nutritious cookie to be delivered to children attending public primary schools. This cookie (28 g) supplies 140 kcal and 2 g protein of a quality superior to 80% milk protein. Currently more than 1.6 million children receive this cookie as a daily snack at a cost of US\$25,000 per million cookies. The purpose of this study was to determine the stability of retinol during the baking process and through the usual shelf life of the cookie in order to assess its relevance as a source of vitamin A.

Three batches of cookies were produced following standard procedures but using a premix of corn soybean flours containing 96 µg/g retinol palmitate in beads, plus iron and complex B vitamins. Total retinol content was calculated before and after baking and after different periods of storage at room temperature (25°C and 70-80% relative humidity). A specific HPLC method was developed for this purpose.

Nine percent of retinol was lost during baking and the cookie conserved 95, 83, and 76% of its initial retinol content after 15, 30, and 45 days respectively. Considering that its shelf life is 45 days, the cookie is an excellent vehicle for vitamin A. Total cost of fortification process to supply at least 50% RDA of vitamin A for children (400,500 RE) is US\$180 per million cookies, or 0.77% of the total cost of the cookie. That means US\$0.027 per child during the 150-day school year. Therefore, vitamin A can be provided efficiently by fortifying bakery products targeted to specific groups.

#### Biologic Significance of Vitamin A Deficiency Infection

#### Oral Presentations

#### VITAMIN A STATUS AND SUPPLEMENTATION AND ITS EFFECT ON IMMUNITY IN CHILDREN WITH AIDS

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An association between vitamin A deficiency, immune dysfunction and common childhood infections is well recognized. However, data on children on the relationship between vitamin A status and AIDS, and the effects of vitamin A supplementation are lacking. The objectives of this study involving children with AIDS were to determine the relationship between vitamin A, immune and nutritional status and the effect of high dose vitamin A supplementation on immune status. The study was a randomized double-blind placebo-controlled clinical trial. Children with AIDS attending the HIV clinic at the Children's Hospital in 1994/5 were randomized to receive either vitamin A 200,000 IU on two successive days or placebo. Children with acute infections or fever (>37.5°C) were excluded. Clinical, biochemical and immunological investigations (flow cytometry and immunoglobulin levels) were done prior to enrolment and four weeks later. Vitamin A levels were determined by HPLC. Children were classified into three immunological categories: no moderate and severe suppression on the basis of CDC criteria (CD4 counts). Seventy-five children were enrolled into the study. The median (25-75th centile) age was 17 (9-26) months, 37% being <1 year old, percent weight for age was 77 (66-88), 13% being <60 and 53% <80% of expected, and vitamin A level was 19 (9-26) µg/dl with 12% <10 and 50 <20 µg/dl. Most children (41/54, 76%) were severely immune suppressed according to CDC criteria while 23 (30.7%) were moderately suppressed and 11 (14.7%) had no suppression. There was a positive correlation between vitamin A level and CD4 counts ( $r = 0.39 < 0.18 < 0.57$ ) and a negative correlation with IgG level ( $r = 0.43 < 0.22 < 0.01$ ). No correlation with nutritional status and age was noted. Comparison of the study and control groups revealed no differences in their baseline age, nutritional or vitamin A status. However, children who received vitamin A ( $n = 36$ ) were more immune suppressed than the placebo group ( $n = 39$ ) ( $p = 0.01$ ). Vitamin A supplementation was associated with increased vitamin A levels ( $p = 0.04$ ) and improved immune function four weeks later as manifested by increased absolute lymphocyte ( $p = 0.05$ ), CD4 ( $p = 0.03$ ), CD56 ( $p = 0.05$ ) and CD29 counts ( $p = 0.07$ ). No such effects were noted in the placebo group. In conclusion, severe immune suppression in children was associated with a lower vitamin A level which was independent of nutritional status and age, and in the short term, high dose vitamin A supplementation improved immunological function. The data supports the use of vitamin A therapy in the standard case management of children with AIDS.

#### EFFECT OF VITAMIN A SUPPLEMENTS IN REDUCING SEVERITY OF LOWER RESPIRATORY INFECTION AMONG CHILDREN IN TANZANIA

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Administration of vitamin A supplements has been associated with reduced mortality among preschool children in a number of studies, but was without effect on the incidence of childhood infections. A possible explanation for this apparent discordance may be that the supplements reduce the severity but not the incidence of infections. To examine this hypothesis with respect to acute lower respiratory infection (ALRI) we carried out a randomized, double-blind placebo-controlled trial to determine whether the administration of vitamin A reduces the severity of ALRI among pre-school children who are admitted to hospital.

The study was carried out at Muhimbili Medical Centre, Dar es Salaam, Tanzania. We enrolled 625 children between the ages of 6 months and 6 years with clinically diagnosed ALRI. All subjects were free of night blindness and severe malnourishment. At enrollment, children received 2 doses of placebo or 2 doses of 200,000 IU (or 100,000 IU for infants) of vitamin A (one dose on two successive days) in addition to standard ALRI treatment. Children were examined daily by a pediatrician and vital signs (respiratory rate, temperature, heart rate) were assessed every 6 hours. Oxygen saturation was assessed daily. Background characteristics (socioeconomic status, etc.) were collected. Assessment of diet prior to admission was carried out using a food frequency questionnaire. After discharge from hospital, each child was followed up every 2 weeks for 1 year to examine the effects of vitamin A supplementation on recurrence of ALRI, and the occurrence of other infections. Results of the hospital phase of the study, which was completed in July 1995 will be presented.

Supported by the Thrasher Research Fund and the International Development Research Center

**THERAPEUTIC IMPACT OF VITAMIN A ADMINISTRATION DURING ACUTE DIARRHEA.** Bhandari N [Bahl R](#) Sazawal S Bhan MK. Division of Gastroenterology and Nutrition Department of Pediatrics All India Institute of Medical Sciences New Delhi India

Vitamin A supplementation in children has been shown to reduce the prevalence of severe diarrhea over the subsequent few months. We therefore examined the impact of supplementation with vitamin A during acute diarrhea on the episode duration and severity.

In a double blind controlled field trial 900 children 1-5 years of age with acute diarrhea of  $\leq 7$  days duration were randomly assigned to receive vitamin A (200,000 IU) or placebo. They were followed up at home every alternate day till recovery from the diarrheal episode.

In all study children, those vitamin A treated had a significantly reduced risk of persistent diarrhea [Odds ratio (OR) 0.30, 95% confidence interval (CI) 0.07-0.97] but there was no such impact on the mean diarrheal duration or the mean stool frequency. In the subgroup of children who were not breast fed the mean diarrheal duration (Ratio of Geometric Means (GM) 0.84, 95% CI 0.72-0.97), mean number of stools passed after the intervention (Ratio of GM 0.73, 95% CI 0.56-0.95), the proportion of episodes lasting  $\geq 14$  days ( $P=0.002$ ) and percent children who passed watery stools on any study day (OR 0.40, 95% CI 0.21-0.77) were significantly lower.

Administering vitamin A during acute diarrhea may reduce the severity of the episode including the risk of persistent diarrhea in non breast fed children. Similar benefit was not seen in breast fed children in this study.

## Oral Presentations

## Dietary Interventions

**CRUCIAL ELEMENTS IN A HOME GARDENING PROJECT: EXPERIENCE FROM A NATIONWIDE PROGRAM IN BANGLADESH.** [Tahukder A](#), Khan T A Baker S K, Bloem M W. P O Box 6066 Gulshan Dhaka 1212 Bangladesh

For the past 8 years, HKI has promoted a large scale home gardening program that has covered poor households in 90 rural sub districts of Bangladesh. This program which began as a pilot project involving 150 families, now targets more than 360,000 households throughout the country. The project includes a system to collect quantitative data to monitor project activities. From the activities monitoring system and project experience, key elements have been identified as being crucial to successful home gardening.

The first element is to maintain the production of vegetables at high levels throughout the year. The monitoring system collects data on seasonal production of vegetables and consumption of vegetables over a three-day period. Members of households with gardens that produced vegetables throughout the year ate a significantly greater amount of vegetables (646 grams) than members of households with gardens that did not produce vegetables through the year (451 grams). This evidence is consistent with the likelihood that home gardens that produce vegetables throughout the year have a positive influence on consumption of vitamin A rich foods.

Secondly, community based services to support home gardeners are essential for them to increase their production of vegetables. Community based services to provide essential supplies such as seeds, seedlings and saplings tend to encourage the production of vegetables and fruits throughout the year. Project experience suggests that community members, especially poor women with limited opportunities to earn their own income, can be trained to effectively produce high quality seeds in a nursery thereby spreading gardening to other community members who purchase seeds from nursery holders for their own home gardens. All of the nursery holders were able to produce high quality seeds. Moreover, 24% were able to produce 6 or more varieties of seeds.

The third element is that it is not sufficient to promote one vegetable alone. Greater choice is likely to improve children's consumption of vegetables. Members of households that produced a greater variety of vegetables consumed more vegetables than households that produced fewer varieties of vegetables.

The last key issue is to incorporate sustainability into the project. HKI experience has been that the technology needed for successful home gardening is not expensive. As the project continues, HKI will be able to explore the hypothesis that community members appreciate that improved inputs lead to improved production and therefore will be motivated to continue this activity because of additional earnings.

**Does the production of dark green leafy vegetables and fruits play a role in the etiology of maternal night blindness, diarrhea and malnutrition in Bangladesh?** [Martin W. Bloem](#), Nasreen Huq, Jonathan Gorstein, Susan Burger, Tabibul Kahn, Nael Islam, Shawn Baker, Frances Davidson (HKI USAID)

Vitamin A deficiency is considered as a public health problem in Bangladesh and a universal biannual distribution of high dose vitamin A capsules has been in place over the past two decades. Although this program is beneficial for preschool children, Bangladesh has been seeking more sustainable approaches for the entire population. Since 1993, Helen Keller International has been implementing a large scale home gardening promotion project. In order to measure the potential impact of such a program, a community intervention trial has been integrated as part of the program design.

This study reports baseline data from a total of 7,382 women of reproductive age. In two logistic models, vitamin A intake above the median was significantly associated with indicators for homestead gardens after adjusting for various socioeconomic indicators.

Of the women studied, 3.2% (95% CI = 2.8-3.6) reported being night blind at the time of the interview. Adjusted for house size, number of children under 6, age, agriculture land size of the homestead, maternal education, family size and oil consumption, vitamin A intake ( $> 400$  RE, OR = 0.55, 95% CI = 0.41-0.75,  $P < 0.0000$ ) was significantly associated with maternal night blindness. After adjusting for possible confounding factors, vitamin A intake above the median was significantly associated with a decreased risk of diarrhea (OR = 0.62, 95% CI = 0.48-0.82,  $p < 0.0000$ ) and a normal body mass index ( $BMI \geq 18.5$ ) (OR = 1.15, 95% CI = 1.04-1.27,  $p = 0.0074$ ).

This study provides evidence that dietary vitamin A intake is associated with home production of dark green leafy vegetables and that relatively higher intake of vitamin A is associated with a decreased risk of maternal night blindness, diarrhea and maternal chronic energy deficiency. Despite potential low bioavailability of beta carotene in dark green leafy vegetables, promotion of production and consumption of these products seems to be valuable in those countries where there are no alternative sources with a higher bioavailability of vitamin A.

### Provitamin A Carotenoid Content of Common Foods

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Use of locally available carotene rich foods is accepted as a long term sustainable strategy to combat vitamin A deficiency (VAD). One of the limitations to developing food based interventions is lack of reliable data on provitamin A carotenoid content of foods. Studies were therefore undertaken to determine the carotenoid profile of a wide variety of Indian foods using HPLC technique. Analysis of green leafy vegetables showed that Beta-carotene (BC) is the most predominant provitamin A. Besides the conventional vegetables leaves of many less familiar and region specific plants were found to be good sources of BC. Some of the newer varieties of amaranth, carrot and sweet potato contain significantly higher concentration of BC than the traditional varieties. Selective propagation of such high carotene foods through horticulture programs would go a long way in combating VAD. Apart from cultivar differences, carotene content of vegetables varies with the stage of maturity, season and application of chemicals. For instance, BC concentration of vegetables was found to be higher in winter than in summer. Processing and cooking also have a significant impact. Our studies showed that cooking with a lid, sauteing with oil and adding lime juice or tomato to the recipes help in the retention of BC. While prolonged cooking, as in the preparation of carrot/pumpkin sweets, causes considerable loss in carotene. Pickling, a common method of food storage, also results in variable losses. This information is useful not only for accurate assessment of dietary intake of vitamin A, but also for nutrition communication programs to promote appropriate methods of preparation to minimize carotene losses.

DIETARY SOURCES OF VITAMIN A WEIGHED FOOD INTAKES OF PRESCHOOL AGE CHILDREN IN RURAL CENTRAL JAVA, INDONESIA. Th Ninuk SH (1) MJ Dibley (2) S Dawiesah Ismadi (3) M Serdula (4) CL Kjolhede (2) T Sadjimin (3) (1) Nutrition Academy Yogyakarta Indonesia, (2) Johns Hopkins University Baltimore USA (3) Gadjah Mada University Yogyakarta, Indonesia, (4) Division of Nutrition Centers for Disease Control Atlanta, USA

Quantitative information about the level of vitamin A and sources of dietary vitamin A of preschool age children is an important preliminary step to designing appropriate community based dietary interventions to prevent deficiency. As part of the Dietvita study a community based assessment of dietary intake of vitamin A was conducted using weighed food intakes and a stable isotope method to measure breastmilk volumes. The objective was to quantify the level of vitamin A intake and identify the various sources of vitamin A in the diets of preschool age rural children. The data was collected from a sample of 296 children aged 6 through 47 months at enrollment, over a two year period starting in October 1990. During this survey period average two weekly breastmilk intake was measured in 94 children using a deuterium oxide method. Breastmilk vitamin A was measured using standard HPLC methods. Nutrient intakes were calculated using the International MinList database. A total of 1776 days of observation provided information about 30321 eating events involving 15069 recipes & 3053 foods. Average vitamin A intake across all ages was 201 RE/day with a slightly higher level of intake (245 RE/day) in children 6 to 11 months. Breastmilk vitamin A accounted for 67% of vitamin A intake of children less than 12 months, 65% for those aged 12 to 23 months and 36% for those aged 24 to 35 months. The major sources of vitamin A for children over 24 months were eggs/milk (31% of dietary vitamin A intake), fruits (30%) & green leafy vegetables (9%). There were no differences in vitamin A intake by gender.

### Biologic Significance of Vitamin A Deficiency: Growth and Inflammation

### Oral Presentations

REDUCTION IN SERUM RETINOL AND URINARY LOSS OF VITAMIN A IN CHILDREN WITH ACUTE DIARRHEA. J.O. Alvarez, E Salazar-Lundo, C.B. Stephensen, J. Santisteban, A. Colarossi and S. Blount. University of Alabama at Birmingham, AL 35294-0008 and Universidad Peruana Cayetano Heredia (UPCH) Lima, Peru

Acute diarrhea, pneumonia and sepsis have been shown to cause urinary excretion of retinol and retinol binding protein (RBP). This study included 101 children 1-2 yr old admitted for treatment of acute diarrhea to UPCH Rehydration Unit. Urinary loss of retinol/RBP was observed in 86% of the children at the time of admission. Excretion continued daily through the period of hospitalization while diarrhea was still present. Of the 16 children still hospitalized on day 5, 63% continue to excrete significant amounts of retinol/RBP in the urine. Rotavirus infection ( $p=0.001$ ) and history of fever ( $p=0.042$ ) were associated with excretion. Reducing substances ( $p=0.0001$ ) and glucose ( $p=0.0001$ ) in the stools (the markers for severity of rotavirus infection) were strongly associated with retinol excretion and showed a dose response relationship.

Urinary excretion of retinol/RBP was positively correlated with urinary total protein, urinary  $\alpha$  acid glycoprotein and serum concentration of  $\alpha$  acid glycoprotein (an acute phase protein) and negatively correlated with the ratio of serum transthyretin (TTR) to RBP (i.e. TTR/RBP). Large excretions were observed predominantly in children with a serum TTR/RBP  $<1$ . A lower serum TTR/RBP ratio indicates an increase in the level of uncomplexed (low molecular weight) RBP-Retinol which can filter through the glomerulus in significant amounts and may exceed the reabsorptive capacity of the tubuli of the kidney, thus leaking into the urine. Interestingly, serum retinol levels ( $\mu\text{mol/l} \pm \text{SD}$ ) decreased as a function of duration of diarrhea (day 1  $n=104$ ,  $0.54 \pm 0.23$ ; day 3  $n=55$ ,  $0.42 \pm 0.16$ ; day 5  $n=12$ ,  $0.37 \pm 0.22$ ). In a subset of 52 children who had diarrhea for more than 3 days, their serum retinol dropped from  $0.53 \pm 0.23$  on day 1 to  $0.43 \pm 0.17$  on day 3.

These results indicate that acute diarrhea is accompanied by a reduction in serum retinol and a concomitant excretion of retinol/RBP in the urine. Although a cause-effect relationship has not been demonstrated yet between these two phenomena, they are both associated with the acute phase reaction. Depletion of vitamin A stores and progression to persistent diarrhea are two likely consequences of these phenomena.

Epidemiology of Night Blindness During Pregnancy in Rural Nepal. P. Christian, KP West Jr, SK Khatri, J Katz, RJ Stoltzfus, RP Pokhrel. Center for Human Nutrition and Dana Center for Preventive Ophthalmology, Johns Hopkins Univ, Baltimore, MD 21205 and The National Society for the Prevention of Blindness, Kathmandu, Nepal

Very little is known about the epidemiology and natural history of night blindness (XN) of pregnancy. In rural Nepal, XN occurs in an estimated 10-20% of pregnant women. Risk factors of XN during pregnancy were assessed using a matched case control design in the south eastern plains of Nepal where a randomized clinical trial is underway supplementing women of reproductive ages with low dose vitamin A or  $\beta$  carotene to determine its impact on pregnancy outcome and early infant survival. Cases were identified through a surveillance system and verified by additional probing. Controls were randomly selected from non XN pregnant women matched for gestational age. Cases and controls ( $N=90$  pairs) were interviewed and examined at home soon after being identified. Nutritional assessment included estimation of serum retinol, hemoglobin and anthropometric status and food frequency intake.

Matched pair analyses revealed that controls were more likely to have consumed milk (Odds Ratio=2.4, 95% CI 1.2-4.8), whey (OR=2.1, 95% CI 1.1-4.4), mangoes (OR=7, 95% CI 1.2-42.3) and dark green leaves (OR=2.4, 95% CI 1.3-4.6) in the previous week. Serum retinol of cases was  $10 \mu\text{g/dl}$  lower than the controls ( $p<0.0001$ ) and was associated with intakes of vitamin A foods. Weight (by 2.2 kg), mid arm circumference (by 0.7 cm) and Hb levels (by 0.76 g/dl) were also significantly lower in cases. XN women were more likely to report a poor appetite (OR=3.0, 95% CI 1.3-6.8), nausea (OR=3.0, 95% CI 3.5-7.3), diarrhea (OR=3.0, 95% CI 1.1-7.8), painful urination (OR=2.2, 95% CI 1.1-4.4) and lower abdominal pain (OR=2.0, 95% CI 1.1-3.7). XN during pregnancy appears to be related to vitamin A deficiency, anemia and increased risk of morbidity, thus posing a significant risk to women's reproductive health and nutrition. Funded by USAID Office of Health & Nutrition, Washington DC.

**ACUTE RESPIRATORY INFECTIONS PREVENT IMPROVEMENT OF VITAMIN A STATUS IN YOUNG INFANTS SUPPLEMENTED WITH VITAMIN A** M. Mujibur Rahman, D Mahalanabis J O Alvarez M A Wahed M A Islam D Habte M A Khaled International Centre for Diarrhoeal Disease Research Bangladesh and Departments of International Health and Nutrition Sciences University of Alabama at Birmingham AL 35294 USA

At immunization contact 165 infants 2½ months old were randomly assigned to receive either 15 mg vitamin A (retinyl palmitate) or placebo. Three such doses were given at monthly intervals with each diphtheria pertussis tetanus and oral polio (DPT/OPV) immunization dose. The diarrhea and acute respiratory infection (ARI) morbidity was similar in the vitamin A and placebo groups. However, the duration (days/child year mean±SD) of ARI was less in the vitamin A group compared with placebo group (27.6±17.1 vs 40.8±22.7 p=0.005). Fasting retinol concentrations were measured at entry and in 61 infants, the relative dose response (RDR) test was done one month after the third vitamin A dose. Eighty-eight percent of the infants had serum retinol concentration <0.70 µmol/L at entry. After 3 months, the serum retinol levels improved significantly in both groups and in the vitamin A supplemented group, the serum retinol concentration was significantly better than that in the placebo group (p=0.02). However, 61% of the infants remained deficient despite vitamin A supplementation. Among vitamin A supplemented infants, only diarrhea and ARI morbidity during the 3-month period were compared in children with normal versus children with abnormal RDR at the end of the supplementation period. ARI episodes were more frequent in the supplemented infants who remained vitamin A deficient at the end of the 3-month period (p=0.027). Also, the cumulative duration (days mean±SD) of fever and cough was 5.0±2.8 in the normal versus 11.2±6.0 in the deficient group (p=0.04). The results of this study suggest that a large proportion of infants remain vitamin A deficient even after large dose vitamin A supplementation because of frequent respiratory infections, particularly those accompanied by fever.

Oral Presentations

Using Ethnographic Methods in Vitamin A Deficiency Research

**FOCUSED ETHNOGRAPHY FOR COMMUNITY ASSESSMENT OF NATURAL FOOD SOURCES OF VITAMIN A** HV Kuhnlein GH Pelto LS Blum PJ Pelto and Members of IUNS Committee II 6 (1992-94) Centre for Nutrition and the Environment of Indigenous Peoples McGill University Montreal Quebec Canada and Dept of Anthropology University of Connecticut Storrs CT USA

Providing vitamin A as natural food available in communities is viewed as an effective long-term strategy for the alleviation of vitamin A deficiency. However, there are notable difficulties in understanding the complexities of what food is available, what are its vitamin A contents, how much is eaten, and why it is eaten, as well as understanding the beliefs and behaviors specific to clinical vitamin A deficiency. A systematic procedure to gather this information was created by drawing on tools and techniques from the disciplines of anthropology and nutrition. The procedure addresses food identified in the local food system, cultural beliefs influencing consumption by women and young children, ecological, economic, and cultural constraints to the use of vitamin A rich food, and local understandings of deficiency. Tools included community food sources data tables, food frequency market survey, key informant interviewing, belief and behavior mapping, and structured interviews. Field teams evaluated the procedure in Canawan, Philippines including wet and dry seasons, Cajamarca, Peru including rural and suburban areas, a rural village in Niger, Douman Village, PRC, and Shenguda Village in Andhra Pradesh, India. This diversity of cultures and environments showed the procedure effective and able to provide essential information for food promotion programs for vitamin A deficiency prevention. (Sponsored by IDRC 92-0224-00)

**BELIEFS AND BEHAVIORAL FACTORS AFFECTING VITAMIN A DEFICIENCY IN NIGER** LS Blum and GH Pelto, Departments of Anthropology and Nutritional Sciences, The University of Connecticut Storrs CT USA

Ethnographic research was conducted in two ecologically distinct areas in Niger to describe beliefs and behaviors affecting vitamin A intake and management of signs and symptoms of clinical deficiency. A two-stage design was used, involving key informant interviewing followed by structured interviews with samples of 100 women in each study site. The paper describes findings reflecting local beliefs and practices for potential health education messages. For example, among cultural concepts of relevance for message development is the belief that the quality and quantity of blood in the body is critical to health, but that blood is highly vulnerable to negative effects of work and illness. The consumption of foods felt to be blood rich, which include liver and fruit and vegetable products rich in vitamin A, is thought to return new blood to the body, thus increasing circulation and positively affecting overall health. Nightblindness is recognized and treated at home with food remedies. However, while appropriate foods are used, the amount and duration of consumption is frequently too short. These findings could facilitate the design of culturally appropriate messages geared to increase the quantity and length of time of intake of home treatments. The study also examined the effects of structural and economic factors influencing care-seeking behaviors. Results illustrate that Hausa tenets dictating gender roles affect treatment practices. For example, women are required to request permission from their husbands to conduct activities beyond the daily routine, leading to a significant waiting period before care is sought for advanced signs of xerophthalmia, which are recognized and considered serious. Since men control household economic resources, women must obtain money from their husbands before accessing treatment, additionally affecting delay in care seeking. These findings indicate that men must be a primary target group in any health-related intervention.

SUSTAINABILITY IN VITAMIN A PROGRAMMES | Darnton Hill P Nestel  
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Vitamin A deficiency disappeared in Europe without the need for specialized programmes presumably through increased affluence and improved nutrition over time. In countries where micronutrient deficiencies are public health problems the need for programmes to continue over a very long time span is essential particularly for iodine and iron but also in poorer populations for vitamin A. Supplementation with capsules was originally conceived as a short term measure but in some countries that need will remain for many years yet. Given the current cost of supplements which most countries cannot afford now without donor assistance questions of sustainability arise. To address this some countries use targeted approaches. However the issue remains that those who get the capsules are often those not most at risk. Fortification is often described as a medium term approach but based on the experience of industrialized countries should be considered a long term intervention. Where the costs are passed onto the consumer and the food industry routinely fortifies food such programmes are potentially sustainable. However there are issues here of the most affluent consumers not being those most at risk of deficiency and the amount of government or donor investment needed to start up programmes. Small scale agricultural approaches including home gardens and the growing of micronutrient rich foods are often described as the most sustainable interventions but these are currently being questioned. Leaving aside the issue of carotenoid bioavailability the evidence for home gardens being sustainable is not impressive. Finally nutrition education is seen as an integral part of program sustainability. However the beneficial impact of nutrition education on micronutrient or vitamin A status is weak although there are a couple of good examples. The OMNI project of USAID is supporting a variety of approaches to combating vitamin A deficiency and intends to evaluate their effectiveness. In the process indicators that enable this to be done in a more rigorous manner will be developed. The development of indirect program based indicators is important because conventional indicators of nutrient adequacy especially biological indicators for vitamin A are relatively insensitive to dynamic changes in the economic and social environment. One example is the income generated from home gardens generally goes to women who spend more on food and who as they become more empowered generally have fewer but better nourished children. Other examples of indirect indicators of program impact on vitamin A status will be developed.

South to South Technical Cooperation as a Sustainable Solution for the Problem of Vitamin A Deficiency | C. Standwaj CRHCS/ECSA Arusha, Tanzania.

South to South Technical Cooperation or Technical Cooperation Between Developing Countries (TCDC) is the provision of technical assistance from one developing country to another often aimed at filling a technical gap/exchange of experience is not only desirable but should be supported as one of the solutions to sustainable elimination of vitamin A deficiency. It is well known that countries are at different levels of development. Therefore TCDC can be a major strategy to share experiences and lessons learnt among developing countries for sustainable virtual elimination of not only vitamin A deficiency but a number of other nutritional problems as well.

South/South Technical Cooperation if effectively planned and supported can bring about sustainable results for the following reasons: a) Adaptability of technical assistance to local conditions is high because of similarities in the socio-economic structures of countries exchanging technical assistance. b) Better appreciation of the political environment can lead to greater commitment for development of approaches upon which further support could be built. Development partners from the North have often prepared programmes for the South without adequate considerations of the South oriented characteristics. These programmes have not been sufficiently internalized and have failed to inspire commitment from countries.

What is sustainability? Sustainability consists of these essential elements: a) Duration of Project to Institutionalize/Internalize project characteristics to inspire commitments and build a Sense of Ownership. b) Institutional and human capacity building. c) Funding that allows for internalization of project characteristics. Flexible Support that allows for a minimum of 5 years for small scale and 10 years for large scale projects.

Opportunities for TCDC Through South/South Technical Cooperation the following could be achieved: a) Sustainable capacity building. Developing genuine rapport and partnerships that build on mutual respect for each other as professional colleagues helps in motivation and ensuring long term support to a project. b) Strengthened institutional framework for project implementation. c) Advocacy for increased government support to ensure continuity and growth. d) Agenda development that is flexible country specific/relevant and adaptable to local situations and realities. e) Develops a sense of ownership of the project among communities. f) human capacity building both in skills and knowledge the framework for project implementation. g) Develop and forge partnerships with Centers of Excellence to build capacities in training research and programme implementation. e.g. CFNI as a relevant Center of Excellence to Africa and strengthening potential centers e.g. ECSA ORANA. g) Virtual Elimination of PEM as a public health problem.

Donors and development agencies should renew their efforts to support TCDC. Support is needed for information and data sharing.

## Other Interventions for Prevention and Control of Vitamin A Deficiency

## Oral Presentations

VITAMIN A STATUS OF ZANZIBARI FIRST-GRADERS: INFLUENCE OF PARASITIC INFECTIONS AND IMPACT OF DEWORMING | RJ Stoltzfus, M Albonico, HM Chwaya, J Tsielsch, L Savioli. Department of International Health, The Johns Hopkins University, Baltimore MD, USA, The Ministry of Health Zanzibar and Programme on Intestinal Parasitic Infections, WHO, Geneva.

Children in Sub-Saharan Africa carry a remarkable burden of parasitic infections and relatively little is known about the influence of those infections on vitamin A status. Furthermore current parasite control strategies use school-based approaches, but there is little information about the magnitude of vitamin A deficiency in school-aged children. In Zanzibar data on vitamin A deficiency have been lacking. Animal sources of vitamin A are rarely consumed and people experience seasonal shortages of food especially vegetables. Xerophthalmia is not noted as a public health problem; other measures of vitamin A deficiency have not been assessed. We recently evaluated the nutritional impact of a school-based deworming program implemented on Pemba Island by the MOH, Zanzibar. For evaluation purposes program and non-program schools were randomly assigned and 12 schools were randomly selected to participate in the program evaluation. The aims of the present study were (1) to measure the prevalence of subclinical vitamin A deficiency (assessed by modified relative dose response MRDR) in first-graders (2) to describe the cross-sectional associations of vitamin A status and parasitic infections and (3) to measure the impact of deworming on vitamin A status. To achieve these objectives we measured the MRDR of 510 first-grade children before the deworming program was started. Twelve months later MRDR was again carried out in 410 of these children. Half of the children were in non-program schools and half received six-monthly deworming as a single 500 mg dose of mebendazole. At baseline 86% were infected with hookworms, 91% with *Trichuris* and 65% with *Ascaris*. Sixty percent were infected with malaria and 37% had detectable hematuria, evidence of urinary schistosomiasis. The vitamin A findings will be forthcoming. (Funded by the USAID Office of Health and Nutrition).

INTEGRATION OF VITAMIN A SUPPLEMENTATION WITH EPI PROGRAMME IN BANGLADESH: AN APPROACH TO INCREASE COVERAGE OF VITAMIN A ADMINISTRATION AMONG INFANTS | R Karim, M Shahjahan, S Begum, S Begum and I Kabir. INFS Dhaka University Children's Nutrition Unit, SCF (UK) Dhaka, Institute of Public Health Nutrition (IPHN) Dhaka, IPHN Dhaka, UNICEF Dhaka, Bangladesh.

An investigation to see the impact of integration of vitamin A (VA) supplementation with the successful Expanded Programme on Immunization (EPI) Programme in Bangladesh was undertaken. Relevant documents were consulted and a few concerned senior staff members were interviewed. During 1989 the vitamin A supplementation coverage rate among the children aged 6 to 72 months was 35%. The coverage for under one year children was 26% during that time. To improve the coverage among the under one year children the programme was integrated with the EPI during 1991 and 50 000 IU of VA were administered at each EPI contact i.e. 6, 10, 14 and 36 weeks of age. Coverage rate increased over 80% but the questions arose of (i) maintenance of required dose and (ii) any toxic effect due to hypervitaminosis. From 1994 the dose has been reduced to 25 000 IU at each contact, and the administration was done at metered dose by pumping method. The coverage during December 1994 was about 79% though the immunization coverage rate was above 90%. The lower VA coverage than the immunization was due to some administrative problems and attitude of field staff. During March/April 1995 National Immunization Day (NID) was observed for mass OPV administration and VA was also integrated with it. The coverage was over 90%.

It can be concluded that, the integration of VA supplementation with a successful programme like EPI can increase the coverage at an optimum level. It is especially important in countries like Bangladesh where the magnitude of vitamin A deficiency even among the infants are high. Administrative factors also play a role in determining the level of output of integration of the two separate programmes.

SAFETY ASPECTS OF VITAMIN A ADMINISTRATION F. Chytil,  
Department of Biochemistry Vanderbilt University School of Medicine  
Nashville TN USA

The popularization of deleterious effects of rather high doses of vitamin A (retinol) and its derivatives the retinoids especially retinoic acid which result in toxic effects including teratogenicity has certainly contributed to the notion among lay people that these compounds are toxic. The same understanding exists among most physicians who were probably at no time during their education instructed that vitamin A has an essential function in organs other than the eye.

In this contribution a different rather unprecedented approach will be described and evidence will be presented to show that retinyl palmitate can be administered safely to such a sensitive group of patients as human neonates. Safety aspects of retinyl palmitate administration will be reviewed retrospectively in two studies.

Since the first study involving prematurely born babies was initiated in 1986 more than 350 very low birth weight babies (below 1300 g) were treated with a repeated intramuscular injection of 2 000 IU. As of this writing none of the treated neonates showed signs of toxicity as for instance bulging of the fontanelle. The fast monitoring of the blood level of vitamin A allowed the attending physician to lower the next dose or to discontinue the dosing if the concentration reaches more than 80 µg/dl.

In the second study another approach was taken when the safety of retinyl palmitate application was evaluated in children suffering from RSV infection. These children were 1 to 6 months old and the administration of retinyl palmitate was oral. Some children were given 12 500 IU or 25 000 IU in a single oral dose. Alternatively some received additionally the same dose 24 hours later resulting in a cumulative value of 25 000 or 50 000 IU. None of the 21 treated children showed any sign of clinical toxicity.

In conclusion based on the two studies it is fair to conclude that vitamin A in the form of retinyl palmitate can be administered in small doses to neonates without any apparent signs of clinical toxicity.

Supported in part by USPHS grant HL 14214 and the Thrasher Fund.

USE OF NUTRITIONAL SURVEILLANCE PROJECT (NSP) TO MONITOR TRENDS IN VITAMIN A CAPSULE DISTRIBUTION  
S K Baker T A Khan A Hye M F Kurwan M W Bloem Helen Keller International P O Box 6066 Gulshan Dhaka 1212 Bangladesh

Vitamin A deficiency has been well documented as a public health problem in Bangladesh. Since the early 1970s high potency vitamin A capsules (200 000 IU) have been distributed twice a year to all children between the ages of 6 months and 6 years.

In April 1990 HKI and a number of partner organizations set up a nutritional surveillance project (NSP) based on sentinel sub districts in rural areas and sentinel slums in urban areas. From the original 10 sentinel rural sub districts and 4 urban slums it has grown to 35 sentinel rural sites, 4 urban slums and 19 partners. The NSP collects information on health, nutrition and socio-economic status from around 18 000 children every two months. Vitamin A capsule (VAC) coverage has been monitored from the inception of the project. The NSP shows that rural distribution is uneven usually ranging from 31% to 57% with coverage in the majority of areas under 50%.

The NSP has proven successful in monitoring changes over time. One important change was a drop in rural coverage to 31% when there was a VAC supply problem due to a change in donors supporting the program. A second was a substantial increase in rural coverage to 87% following the combination of VAC distribution with the second day of a national campaign for polio vaccination for all children under 5. Recently the Government of Bangladesh has built on this initiative to hold a center based National Vitamin A Week and VAC coverage will be assessed through the NSP augmented by an additional survey of urban areas. Results of this special week will be included in the presentation.

Of related interest is the prevalence rates of night blindness among children 24-59 months which vary between 0.6% and 1.8%. Clear seasonal patterns emerge with rates especially high during the October through December period.

## Oral Presentations

## Vitamin A Status Methodology

COMPARISON OF HEPATIC VITAMIN A STORES ESTIMATED BY THE DEUTERATED RETINOL DILUTION TECHNIQUE OR BY ANALYSIS OF HEPATIC BIOPSY SPECIMENS IN BANGLADESHI SURGICAL PATIENTS M J Haskell, G J Handelman, A D Jones, J M Pearson, A Rabbi, M A Awal, M A Wahed, D Mahalanabis and K H Brown. Prog in Int'l Nutrition and Dept of Nutrition Univ of California, Davis, CA; Dhaka Medical College Hospital, Dhaka, Bangladesh; and the International Centre for Diarrhoeal Disease Research, Dhaka, Bangladesh.

Hepatic stores of vitamin A were estimated in 31 adult Bangladeshi surgical patients (M=15, F=16) by the deuterated retinol dilution (DRD) technique and by analysis of the hepatic vitamin A concentration of a liver biopsy specimen obtained during surgery for peptic ulcer or gall bladder disease. Patients ranged in age from 21-65 y and had an average BMI of  $17.7 \pm 3.4$  kg/m<sup>2</sup>. They received 0.753 µmol/kg body weight of d4 retinyl acetate orally 9-11 d prior to surgery. Blood was drawn on the day of surgery and on the day prior to discharge (18-25 d post dose) for measurement of the plasma ratio of retinol/d4 retinol. Hepatic stores of vitamin A were estimated as per Furr et al (AJCN 49:713-6, 1989) using the average of two isotopic ratio measurements. Estimated mean hepatic vitamin A stores were similar by both techniques: 0.098 ± 0.066 mmol (biopsy) vs 0.093 ± 0.052 mmol (DRD). Regression analysis was used to compare results of the isotope dilution technique with analysis of hepatic vitamin A concentrations which ranged from 0.021-0.252 µmol/g. A significant linear relationship was found between the two techniques ( $r=0.69$ ,  $p<0.0001$ ) and the least squares regression line was not significantly different from  $y=x$  ( $p=0.674$ ). Agreement between the techniques was poor in 3 patients who had clinical histories consistent with either poor absorption or retention of the dose of labeled retinol. When these 3 patients are omitted from the analysis the linear relationship is improved even when only a single isotopic ratio measurement is used to estimate hepatic stores ( $r=0.82$ ,  $p<0.00001$ ). Supported by Office of Nutrition, USAID.

VITAMIN A (HOLO-RBP) IN DRIED WHOLE BLOOD SPOTS BY HIGH PERFORMANCE CAPILLARY ELECTROPHORESIS (HPCE)  
J H Humphrey, Yunfa Ma, Yongqin Ma, NE Craft, Div of Human Nutrition, Johns Hopkins School of Hygiene and Public Health, Baltimore, MD, USA; Div of Science, NE Missouri State University, Kirksville, MO; Craft Technologies, Wilson, NC.

We have previously described an HPCE method for analysis of holo-RBP from 2 drops of whole blood collected and air-dried on blood collection filter paper. We have now investigated the effects of several storage conditions (UV light, temperature, duration, and humidity) on stability of the holo-RBP analyte. Thirty fresh blood samples were analyzed for serum retinol concentration by HPLC and spotted on blood collection filter paper (Schliecher and Schuell grade 903). Dried specimens were subjected to the following conditions: 4 levels of temperature (-70°C, -20°C, 4°C, and 25°C) for 1 and 6 months; 3 cycles of freeze-thaw; 365 nm UV light at 24 inches for 1, 4, and 8 hours; storage in sealed plastic bag with and without desiccant at ambient humidity for 3 months; storage in 30% and 90% humidity for 1 and 3 months. Specimens were then analyzed by HPCE and values compared to those obtained by HPLC.

Holo-RBP was stable at  $\leq 4$ °C among specimens stored at room temperature; there was loss in the holo-RBP peak and a new peak emerged. We are currently investigating this new peak to determine if it contains holo-RBP in an isomerized form. Holo-RBP content of specimens stored in sealed plastic with and without desiccant were similar. Specimens were stable at 30% humidity for 3 months, but there were losses after 1 month at 90% humidity. Specimens were stable under the freeze-thaw and UV light conditions tested. (Funded by the Thrasher Research Fund and Office of Health and Nutrition, USAID [Cooperative Agreement No. DAN 0045].)

MODIFIED RELATIVE DOSE RESPONSE (MRDR) TEST FOR THE ASSESSMENT OF VITAMIN A NUTRITIONAL STATUS IN CHILDREN R Manorama N Raghuramulu C Rukmini K Visweswara Rao GNV Brahmam and Vinodini Reddy National Institute of Nutrition Indian Council of Medical Research Hyderabad-500007 AP India

Liver concentrations of vitamin A are commonly used as a measure of vitamin A status. When liver reserves are lower but without any clinical signs a marginal status is known to exist. Several indicators have been suggested to identify this group. More recently a modified relative dose response (MRDR) test has been suggested to be a good indicator. The procedure measures the serum levels of retinol (R) and 3-4 dehydro retinol (DR) 5 hrs after oral dose of DR. The MRDR is calculated as a ratio of DR to R. The present report is to validate this test in undernourished children. A total of 24 children of both sexes in the age range of 5-11 years were studied. After an overnight fast each child was given orally 3-4 dihydroretinyl acetate in oil at the dose of 100 ug/kg body weight. A single venous blood sample was obtained 5 hrs after the dose. Upon completion of the initial test they received either crude palm oil (8 ml = 2400 ug/3-carotene) or retinyl palmitate (600 ug retinol) daily for 60 days and MRDR test was repeated. The results indicated that serum retinol values were significantly related inversely to the MRDR ratio. Based on regression lines and by the point of intersection it was found that MRDR ratio of 0.046 is the cut off as indicator of adequacy or inadequacy in vitamin A nutritional status. All the children were found to have less than 0.046 MRDR after treatment with vitamin A or red palm oil indicating the adequate tissue stores. It may thus be concluded that MRDR is a good indicator of vitamin A nutritional status.

CASUAL VS FULL BREASTMILK EXPRESSION EFFECTS ON MEASUREMENTS OF VITAMIN A AL Rice RJ Stoltzfus <sup>1</sup>CL Kjolhede <sup>2</sup>A de Francisco <sup>2</sup>MA Wahed <sup>2</sup>J Chakraborty <sup>1</sup>The Division of Human Nutrition The Johns Hopkins University School of Hygiene and Public Health Baltimore MD USA <sup>2</sup>International Centre for Diarrhoeal Disease Research Dhaka Bangladesh

During the enrollment round of a community based maternal vitamin A supplementation study of lactating women (2 ± 1 wk postpartum) in Matlab Bangladesh we randomized study participants to two methods of breastmilk collection. For casual breastmilk collection mothers (n=110) manually expressed < 5 mL of breastmilk during their home visits (median time of collection=1145 h range 0920-1735). For full breastmilk collection mothers (n=110) came to a clinic where a manual breast pump was used to express the entire contents of one breast which had not been used to feed an infant for ≥ 2 h (median time of collection=1200 h range 1045-1355). All milk samples were analyzed for their fat content using the creamatocrit test and for vitamin A using HPLC techniques.

The time postpartum, time of day of sample collection and time since last feed all influence the fat and therefore the vitamin A content of individual breastmilk samples. A challenge in designing population-based surveys of breastmilk vitamin A content is that one must either obtain a representative sample of milk or else control for the variation in fat content. Expressing vitamin A content as a ratio to milk fat is a promising strategy for controlling for this sampling variation. We will report whether population results from full breastmilk expressions differ from casual samples of milk after controlling for milk fat content.

The use of breastmilk vitamin A content as an indicator of vitamin A status at the community level has recently been receiving increasing attention. However appropriate methods for breastmilk sample collection and analysis have not yet been extensively tested. The results from this study will have practical implications for those planning such population-based studies in the future. (Funded by USAID Office of Nutrition)

EVALUATION OF PARAMETERS OF VITAMIN A STATUS USING DATA FROM BREASTFEEDING AND NON BREASTFEEDING WOMEN S de Pee Y Yuniar C E West Muhlar Department of Human Nutrition Wageningen Agricultural University The Netherlands and Nutrition Research and Development Centre Bogor Indonesia

Data from a cross sectional study (unpublished) and an intervention study (The Lancet 1995 346 75 81) in breastfeeding and non breastfeeding women in West Java were used to answer the following questions on vitamin A status parameters

- \* Breastmilk retinol content
  - 1 Does milk retinol concentration depend on the age of the breastfed child?
  - 2 Should milk retinol concentration be expressed per volume or gram milk fat?
- Modified relative dose response (MRDR) method
  - 3 How sensitive is the MRDR method to detect marginal serum retinol levels?
  - 4 Does the MRDR method behave differently in breastfeeding and non breastfeeding women?
- Detecting change in vitamin A status
  - 5 Which parameter is most sensitive for detecting a difference in change of vitamin A status?

We have found the following answers to those questions

- 1 The concentration of retinol and of fat in milk were both lower in women with a breastfed child younger than 7 mo (n=67) as compared to those with an older child (n=108). The retinol content of milk fat was the same for all women which was also true for serum retinol content.
- 2 The difference in change as found in the intervention study between the enriched wafer and the control wafer group required 36 and 139 women per group when milk retinol concentration was expressed in terms of volume and of fat respectively. Thus in terms of volume is better.
- 3 Of 99 breastfeeding women with serum retinol < 0.70 μmol/L 26% had a MRDR ratio indicating normal vitamin A stores (< 0.06). Such a difference cannot be explained by low retinol binding protein (RBP) levels or infection.
- 4 Breastfeeding women had a significantly lower serum retinol concentration for a given DR/R ratio than non breastfeeding women. This raises the question whether different cut off values should be used for different population groups.
- 5 The difference between the enriched wafer and the control wafer group could have been detected for breastmilk retinol concentration. MRDR method serum RBP and serum retinol with groups of 6, 53, 35 and 19 women respectively. For this population with baseline serum retinol levels of 0.85 μmol/L serum retinol was thus the most sensitive to detect a difference in change of vitamin A status.

INDIRECT CONTROL FOR THE MARKETING OF FORTIFIED FOODS SUGAR WITH VITAMIN A AND SALT WITH IODINE THROUGH MICRONUTRIENT CANTONAL SCHOOLS N Ramirez Nutrition Program UNICEF and THE MINISTRY OF EDUCATION Guatemala City GUATEMALA

Guatemala initiated a sugar fortification program with vitamin A in the early 70s becoming the pioneer in this field. However, the program did not include an effective monitoring and control system in order to determine in what condition fortified foods reached the population. In 1992, after an initiative launched by the San Carlos University in Guatemala and the Congress, the law that regulates food fortification was revised and Decree 44-92 with its subsequent regulations were promulgated and are currently in effect. The Ministry of Education approved the creation of an indirect control system for the marketing of fortified foods with technical assistance from UNICEF and support from the National Commission on Food Enrichment and Fortification, which was created to ensure enforcement of the law. From the total official rural schools scattered in the 22 departments of the country, 417 micronutrient sentinel schools were randomly selected. Teachers were trained on the importance of fortified foods consumption, the implications of deficiency, prevention measures, and sample recollection, registration, and submission. A random sample of 20 children who provided sugar and salt samples from their homes was established in every school. The study had a duration of one year with active participation from the decision-making level: the regional directors, supervisors, school principals, teachers, students, and their families, achieving an excellent level of reception of program messages. The samples were analyzed in laboratories from INCAP. The results obtained help to determine the level of fortification contained in sugar and salt reaching the homes and the amount of micrograms ( $\mu\text{g}$ ) of retinol and parts per million (ppm) of iodine that these children are consuming. Preliminary analysis shows that 67.49% of sugar samples have less than 10  $\mu\text{g}$  and from these 33.4% are under 5  $\mu\text{g}$ , 27.1% are between 10-20  $\mu\text{g}$ , 5.4% are over 20  $\mu\text{g}$  and only 0.01% do not contain retinol. Even though the sugar fortification process has received improvements, it is necessary to join forces in order to optimize the program. In the case of iodized salt, 30.6% of the samples meet the levels determined by law (30-100 ppm), 57.8% are under 30 ppm and from these 34.8% show levels under 15 ppm, 1.8% are over 105 ppm and only 9.8% do not contain iodine.

IDENTIFICATION OF CULTIVARS OF A WIDELY CONSUMED MESOAMERICAN SQUASH OF HIGH  $\beta$ -CAROTENE CONTENT F Vasquez, B Barrientos, E Pretzanzin, E Carrillo, A Morales, K Molina, R Benavides, y O Dary, School of Agronomy, Universidad de San Carlos de Guatemala and Institute of Nutrition of Central America and Panama (INCAP), Guatemala City, Guatemala.

Infants (1-3 years old) are the most at risk group to suffer vitamin A deficiency. Fortification of staple foods is insufficient to guarantee coverage of this group. Therefore, promotion of appropriate vitamin A-rich waning foods is needed. A Mesoamerican squash (*Cucurbita sp.*) is widely utilized in Guatemala and neighboring countries as one of the most common foods introduced early in the weaning period. The purpose of this study was to identify cultivars of this kind of squash whose fruits fit consumer predilection and at the same time are good sources of  $\beta$ -carotene. It is expected that agronomic characteristics of the promising cultivars could be further improved through genetic breeding.

Twenty squash cultivars were selected from production regions in highland Guatemala. Seeds from these cultivars were planted simultaneously following a rectangular 4 x 5 frame with 3 replicates in the farms located on the Universidad de San Carlos campus. Fifty-seven variables (31 quantitative and 26 qualitative) were studied, including agronomic properties, consumer preferences, and fruit content of  $\beta$ -carotene and other nutrients.

Consumers preferred flat-shaped, medium to large-sized fruits with deep ribs, a smooth and large ring left by the flower structure, and with dark orange flesh. The latter trait was associated with the  $\beta$ -carotene content, which varied from 10 to 60 RE/100 g fresh weight. Four cultivars were identified as promising for further genetic improvement because they showed good economic and agronomic features as well as an adequate  $\beta$ -carotene content (40 RE/100 g).

A NOVEL AND SIMPLE QUANTITATIVE METHOD TO DETERMINE RETINOL IN FORTIFIED SUGAR K Molina, O Dary, M Guamuch, and G Pirir, Institute of Nutrition of Central America and Panama, Guatemala City, Guatemala.

Analytical methods to determine micronutrients are required for the quality control and quality assurance of food fortification programs. Quantitative methods are preferred because of their accuracy and precision. However, sometimes these methods are too complicated or laborious to be practical, and they are replaced by semi-quantitative alternatives. This has been the case for vitamin A fortified sugar. The existent quantitative assays are based on retinol extraction by organic solvents which are volatile and explosive, especially in warm conditions typical of the region where sugar mills are located. The purpose of this study was to develop a quantitative method to determine retinol in sugar, avoiding the use of hazardous solvents.

The new method uses a Sep Pak cartridge containing a C-18 resin. Retinol binds to the hydrophobic resin, which replaces extraction with solvents. Weakly bound and interfering substances from sugar are eluted with 50% isopropanol. Then, retinol is released with pure isopropanol and quantified by means of its absorbance at 325 nm in a UV/Visible spectrophotometer.

The method shows perfect linearity up to 90  $\mu\text{g/g}$  with detection and quantification limits of 0.3 and 1.0  $\mu\text{g/g}$ , respectively. The intra-assay variability is 5.2 ± 1.5% and the inter-assay variability is 13.6 ± 1.7%. Values of these parameters are better or similar than those of current methods. Recovery is lower (76% compared to 90-95%) than the methods based on extraction by solvents. However, once the results are corrected with the proper recovery factor, which is reproducible, they are reliable. The practical applicability of this method under mill laboratory conditions still needs to be confirmed.

BY PRODUCTS OF THE REFINING OF AFRICAN PALM (*Elaeis guineensis*) OIL AS A SOURCE OF CAROTENOIDS AND FAT A Molina Cruz, R Perez, E de Mejia, C de Bosque, M Selle, and R Biessani, Universidad del Valle de Guatemala, INCAP, Guatemala City.

Raw palm oil (RPO) and its refining soapstock waste are rich sources of  $\beta$ -carotene. The effect on carotenoids of storage or acidulation of soapstocks to convert them into edible fatty acids was studied together with the use of the fatty acids in the diet of laying hens. RPO and its soapstocks were found to contain 550 ± 32 and 286 ± 22 ppm total carotenoids (dry weight); these decreased 36% and 48% after one year of storage at room temperature. Soapstock acidulation did not change total carotenoids significantly. High performance liquid chromatography (HPLC) analysis detected less carotenes in the oil by products compared to RPO, but no change was detected in carotenoid composition due to acidulation. In RPO, 64 ± 2% of carotenoids were beta-carotene, while 53 ± 4% and 46 ± 6% were beta-carotene in soapstocks and fatty acids, alpha-carotene accounted for 20 ± 0.4%, 16 ± 1%, and 19 ± 3% of the carotenoids in the three materials. Duplicated groups of 9 laying hens depleted of carotenoids for 3 weeks received as fat 6, 8, or 10% fatty acids, 6% RPO or 5% animal lard. Carotenoid levels in the diets were 9, 12, and 15 ppm in the fatty acid diets and 33 ppm for the RPO diet. After 3 weeks, the carotenoid levels and pigmentation of the egg yolks for the RPO and fatty acid diets were significantly higher compared to the control with animal lard. There was no detectable change in egg weight or production nor in food consumption during the 3 weeks. Palm oil acidulated soapstocks could be used as a source of carotenoids and fat.

PRETESTING OF VITAMIN A RELATED MESSAGES AND INTERVENTIONS AIMED AT GROUPS AT RISK IN EL SALVADOR. YE Ayala ME Claros\* \*PAHO El Salvador

A formative research about Vitamin A was carried out in two communities of the Paracentral region of El Salvador. Based on this study a communication plan was developed educational messages were designed and materials were adapted to respond to the cultural context and audience being targeted health community personnel and mothers of children under five years old.

The materials included calendar posters recipe cookbooks illustrations and radio programs. The pretesting included interviews and focus groups. The richness of the information was used to adjust the materials as to action plans that will guarantee promotion of practices in the future. Among the subjects included relative value of models regarding clothes expressions colors sizes and mothers' roles and attitudes. In the recordings tone of voices vocabulary duration of dialogue importance of duration of the background music used in messages. Additional relevant aspects mentioned were the influence of local availability of foods and its economic access enabling mothers to incorporate them into the family diet.

All the elements mentioned provided enough details for the design of the communication strategy in the communities. They were also important to implement other interventions such as the promotion of specific food crops and commercial exchange of food products.

Other cultural topics that were originally not considered by the researchers were identified as important factors for the implementation of the program.

Surveys

Poster Presentations

VITAMIN A DEFICIENCY IN THREE MICRONESIAN NATIONS IN THE PACIFIC. Ministries of Health of Kiribati Federated States of Micronesia and Marshall Islands. Jane Paterson and Selma Khan UNICEF Fiji Neal Palafox John Burns School of Medicine University of Hawaii USA

An assessment of the prevalence of vitamin A deficiency (VAD) has been undertaken by a variety of agencies in three Micronesian nations in the Pacific. Findings of population assessments to date are described.

For Kiribati (population 78 300) anecdotal evidence and clinical observations of the ocular signs of VAD began from the early 1980s. In 1989 4 614 children aged 6 months to 5 years were assessed and 14 7% clinical VAD found. A comprehensive control project began in 1991 including 4 monthly capsule distribution to children from 6 months to 5 years. From Ministry of Health records and anecdotally in 1995 the prevalence of clinical VAD has dropped among young children but night blindness among young pregnant women is being increasingly noted.

For Federated States of Micronesia (population 105 900) VAD has been well defined in Chuuk State (population 52 900). In 1989 a statewide survey found that almost 50% of 3-6 year old children had abnormal vitamin A status as measured by conjunctival impression cytology. Serum retinol levels of children 18 months to 6 years assessed as part of a larger study in 1992 confirmed these results.

For Marshall Islands (population 54 700) a 1989 National Nutrition Survey drew attention to VAD. In 1994/5 serum retinol levels of children aged 2-6 years were measured (at Institute of Nutrition College of Physicians and Surgeons Columbia University) and the prevalence of VAD was found to be alarmingly high.

Prevalence of VAD in Chuuk FSM 1992 and Marshall Islands 1994			
Vitamin A Status	Chuuk	Chuuk	Marshall Islands
	18-34 months	3-6 years	1-5 years
	n=218	n=137	n=444
Normal >=20ug/dl	45%	23%	37%
Moderate deficiency 10-19ug/dl	44%	56%	55%
Severe deficiency <10ug/dl	11%	20%	8%

Efforts to coordinate short and long term interventions to address the problems of VAD among island populations living on small low lying atolls and spread across millions of kilometres of ocean present a particular challenge and are ongoing.

NATIONAL VITAMIN A SURVEY IN LAO PDR

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No detailed and countrywide information about vitamin A status has been available for Lao PDR. In April-May 1995 after development of a protocol approved by the MOH UNICEF and WHO two villages from each of 17 Provinces were randomly selected. In each village 100 children aged 0-71 months were due to be surveyed and 20 of their mothers. Indicators of vitamin A status included night blindness for which there are several local terms breast feeding history and 7 day recall of frequency of food consumption (Helen Keller International Food Frequency Method).

The final survey population was 3 376 children aged 0-71 months and 680 of their mothers. Night blindness rate was 0.7% for children aged 24-71 months. Five percent of women of childbearing age were night blind and 5.4% of lactating women. Night blindness was exceptionally prevalent in pregnancy 11.5%. Night blind children and mothers were found in virtually every Province. In a sub sample of children whose eyes were examined one child had Bitot's spots and one child had a corneal ulcer.

Virtually all children were breast fed up to 12 months. On the other hand almost half of the children were already given pre-masticated rice in the first month of life. A third of children had not eaten DGLV during the seven days previous to the survey. Yellow vegetables and fruits were consumed on fewer than three days during the previous seven days by about 75% of children and mothers. Night blind children were significantly less likely to have eaten DGLV or to have been given fried food.

Other factors such as seasonal variation still need investigation. But shortage of vitamin A is clearly putting children and women in Lao PDR needlessly at risk. A Plan of Action focusing on the most vulnerable groups is being implemented.

**PROGRESS OF VITAMIN A DEFICIENCY CONTROL PROGRAMME IN VIETNAM**

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Marjatta Tolvanen, Nguyen Quang Trung, UNICEF Office, Hanoi, Viet Nam

Vitamin A deficiency has long been one of major nutritional problem survey in Viet Nam. This was shown by a study carried out in 1985-1988 by the National Institute of Nutrition (NIN) in collaboration with the Institute of Ophthalmology. The prevalence of active forms of severe xerophthalmia was seven times higher than the WHO cut off point for public health significance. From 1988 with the support of UNICEF a mass distribution of high potency vitamin A capsule campaign has started and expanded over the last four years. Since 1992 the vitamin A capsule have been produced locally.

As a long term strategy nutrition education and promotion of VAC a system that promotes a form of domestic agriculture in which food gardening, fish rearing and animal husbandry are integrated with the support of UNICEF and FAO.

In 1994 a national survey on vitamin A deficiency and protein energy malnutrition was carried out by the NIN with the assistance of UNICEF and Helen Keller International. Result of this survey has shown that the prevalence of clinical xerophthalmia among under 5 children is lower than WHO cut off point for public health significance. Efforts should be continued in order to sustain these success and to reach the goals for the year 2000.

**GREEN LEAVES ARE THE MAIN FOOD SOURCE OF VITAMIN A FOR CHILDREN IN SOME AREAS OF NIGER** H Delisle and S Bakari, Dept of Nutrition, Université de Montréal, Montréal (Que), Canada

Vitamin A (VA) deficiency is a public health problem in most of Sahelian Africa. Information on VA intake and other deficiency risk factors among children is needed for appropriate food based strategies. This study was conducted during the rainy season in 18 villages of Bouza and Ouallam districts in western Niger. Maternal interviews and a food frequency questionnaire were used in a random sample of 470 weaned children aged 2-4 years. All children were weighed and measured. VA status was determined by the modified RDR test in a subsample of 144 children. Median VA intakes were respectively 273 and 677 RE in Bouza and Ouallam ( $p < 0.001$ ). Nearly half the children of Bouza had VA intakes  $< 250$  RE compared with 6% in Ouallam. Median VA intake from green leaves was 78 ER in Bouza and 587 RE in Ouallam and accounted for 36% and 86% of VA intake, respectively. Animal foods provided 35% of total VA intake in Bouza and only 8% in Ouallam. Significant household/maternal indicators of higher VA intake in multivariate analyses were ownership of cattle, fresh green leaf supply in the dry season and maternal awareness of VA deficiency. Although VA intake was much higher the rate of marginal child VA status was as high in Ouallam (77%) as in Bouza (74%). This may partly reflect the higher rates of child morbidity and stunting in Ouallam than in Bouza, two factors that were independently associated with poorer VA status. VA from green leaves contributed positively to VA status although the % of total VA intake from plant foods showed a nearly significant negative association ( $p = 10$ ). The supply of green leaves may therefore compensate for limited access to retinol containing animal products but these preliminary findings are in keeping with the suspected low bioavailability of provitamin A in developing areas where infection and diarrhea are common in children.

**XEROPHTHALMIA PREVALENCE IN TEN DISTRICTS OF THE FAR AND MID WESTERN REGIONS OF NEPAL** Mary Linehan, Ashoke Shrestha, Bharat Ban, and David Nelson, Health and Child Survival Fellows Program, Johns Hopkins University, Baltimore, MD and New ERA, Kathmandu, Nepal, Nepal Vitamin A Technical Assistance Group, Kathmandu, Nepal

A cross sectional survey of 18 920 children 6-60 months was conducted in ten districts of the Far and Mid Western regions of Nepal in two rounds, June-September 1993 and May-August 1994, as part of the Nepal National Vitamin A Deficiency and Control Program of the Ministry of Health. The objective of the survey was to obtain baseline data on the prevalence of xerophthalmia in order to prioritize districts for phased program implementation. A randomly selected sample of children in the survey districts were examined for the presence of clinical signs and symptoms of xerophthalmia and mid upper arm circumference was taken for each child to determine nutritional status.

The prevalence of signs and symptoms of xerophthalmia was XN 1.37%, XB 3.11%, X2 & X3 0.16%, XS 0.41%. Cluster analysis was conducted to determine key predictors of xerophthalmia. Of the 250 clusters surveyed 195 had prevalence of Bitot's spots exceeding 0.5% the WHO/IVACG cut off for a severe public health problem. Bitot's spots were found in all three ecological zones but clusters with the highest prevalence (4% Bitot's spots and higher) were more likely to be located in remote mountain areas where there are long periods of food deficit and terrain areas where there are many landless households. Chronic and severe malnutrition appear to be an important underlying determinant of vitamin A deficiency in Nepal. Boys were at significantly higher risk for Bitot's spots than girls with boys in Humla having nearly twice the risk for Bitot's spots as girls. Regression analysis found the following factors to be associated with increased risk for Bitot's spots: MUAC  $< 12.5$  (OR=2.84), breastfeeding (OR=2.43), maternal literacy (OR=2.10), household vegetable production (OR=1.83), consumption of less than 10 vitamin A rich foods in the last week (OR=1.27) and history of night blindness in the mother (OR=1.39).

Weaning age children are at highest risk for Bitot's spots but risk continues through at least 60 months of age raising important questions about the vitamin A status of adolescent girls and women of child bearing age. Although they are unlikely to exhibit clinical signs and symptoms of xerophthalmia they are likely to have subclinical vitamin A deficiency and inadequate vitamin A stores for gestation and lactation in addition to other micronutrient deficiencies. The prevalence and extent of vitamin A deficiency among women of reproductive age in Nepal should be further examined. Successful program interventions must address maternal nutritional status as well as household food security.

**Assessment of vitamin A deficiency by ophthalmological examination, serum retinol concentration and RDR test in preschool Zairean children** Ph. Donnen<sup>1</sup>, D. Brasseur<sup>1</sup>, M. Dramaix<sup>1</sup>, Bauma Ngoy<sup>2</sup>, P. Mweze Zihandula<sup>3</sup>, F. Vertongen<sup>1</sup>, Ph. Hennart<sup>1</sup>, <sup>1</sup>School of Public Health, Free University of Brussels, Belgium, <sup>2</sup>University Children's Hospital, Queen Fabiola Free University of Brussels, Belgium, <sup>3</sup>University Hospital Saint Pierre, Free University of Brussels, Belgium, <sup>4</sup>Centre de Recherche en Sciences Naturelles (CRSN), Bukavu, Zaire

Vitamin A status was assessed in 415 preschool children selected at random in a rural area in the province of South-Kivu in Zaire by using three methods: ophthalmological examination, retinol serum concentration and Relative Dose Response (RDR) test. The children studied were more stunted than wasted (66.3% versus 12.2%) according to Waterlow classification. Serum concentration of albumin, retinol binding protein and transthyretin were below the lower limit of normally reported values in respectively 16.0, 65.3 and 40.4% of the children. The only ophthalmological signs of vitamin A deficiency were two cases of night blindness which represents a prevalence of 0.68%. Deficient serum retinol concentration ( $< 0.35 \mu\text{mol/L}$ ) was found in 19.7% of the whole study population and in 10.4% of a subsample of children in better nutritional status and non infected (serum albumin concentration  $\geq 35 \text{ g/L}$ , weight for height Z-score  $\geq 2$  and C-Reactive Protein  $< 10 \text{ mg/L}$ ). RDR test realised in a reduced sample of 79 subjects was abnormal for 7.6% of the children but showed a low sensitivity when compared with serum retinol concentration. The implication of these results for the interpretation of serum retinol values and RDR test in populations with a high prevalence of protein energy malnutrition and infection will be discussed.

Supported by a grant from the Fonds de la Recherche Scientifique Médicale (FRSM), contract 3.4505.94 and the Van Buuren Foundation.

### THE VITAMIN A STATUS OF SOUTH AFRICAN CHILDREN 6-71 MONTHS OF AGE RESULTS OF THE NATIONAL SURVEY 1994

The South African Vitamin A Consultative Group (SAVACG)

The paucity of data on the vitamin A status of South African children necessitated this national survey. A national probability sample was drawn with reasonably precise estimates for each province. A total of 360 enumerator sub-districts were studied of which 358 were available for analysis (163 rural and 195 urban). Symptoms of impaired vision and clinical eye signs of vitamin A deficiency were determined according to WHO criteria. Serum vitamin A was determined by HPLC. A total of 18 219 households (19 003 families) were studied. Of the 11 430 children included in the study 6 469 and 4 961 lived in rural and urban areas respectively. A total of 4 788 blood samples were drawn with a similar number from rural and urban areas. The age distribution of the children sampled was fairly consistent across all age groups.

Nationally 12% of children were reported as having night blindness. Bitot's spots were seen in 0.4-0.8%, corneal xerosis in 0.2-0.7% and keratomalacia or corneal scar in 0.1% of children. There was no difference in the prevalence of symptoms and clinical eye signs between rural and urban areas. The mean serum vitamin A concentration of all children was 23.9 µg/dL. The mean concentration of serum vitamin A of children living in urban areas was 15% higher than that of children in rural areas. Biochemically the national prevalence of vitamin A deficiency was present in 3% of the total population. However the national prevalence of marginal vitamin A status (serum vitamin A concentration < 20 µg/dL) was 33% and ranged from 18% in the Northern Cape to 43% in the Northern Province. Marginal vitamin A status was also significantly ( $p < 0.001$ ) more prevalent in the rural (38%) than in the urban areas (25%). A small percentage of children (1%) had a serum vitamin A concentration greater than 50 µg/dL.

The prevalence of marginal vitamin A status was lowest in the youngest children. Children of mothers without formal education or with less than five years of formal education were more than twice as likely to have a low vitamin A status than children of mothers with a standard 10 or higher level of education (Chi square for linear trend = 83,  $p < 0.0001$ ).

In conclusion the findings of this national survey indicate that 1 in 3 children have a marginal vitamin A status. On this basis and according to WHO criteria this survey identifies South Africa as having a serious public health problem of vitamin A deficiency.

### VITAMINE A DEFICIENCY AND CHILDREN FOOD CONSUMPTION BETWEEN THE AGE OF 6 TO 84 MONTHS IN TWO RURAL AREAS OF GUINEA

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A cross sectional study was carried out in May 1995 in two cluster samples of 1500 children selected by chance in two different regions of Guinea (Middle Guinea in the Fouta Djallon Mountains and High Guinea in the east plains) for ophthalmologic examination and anthropometric measurements. Two subsamples of 500 children were selected for mothers interview concerning their child food consumption. The HKI food frequency method was applied and illness related indicators such as diarrhea and fever were recorded.

Prevalence of night blindness was 0.6% in the mountains region and 0% in the plain region. Prevalences of Bitot spot were respectively 0.1% and 0.05%.

Underweight children (< 2 Z scores) were 26.9% in the Fouta Djallon mountains and 27.3% in the east plains. Wasted prevalences were near the same (7% in Middle Guinea and 5.8% in High Guinea) but stunting was less important in Middle Guinea (21.2%) than in High Guinea (35.3%).

The study of weekly consumption of vitamin A rich food revealed that 30.5% of Middle Guinea children ate vit A rich food less than seven times a week and 7.4% never ate any. In High Guinea 10.4% ate less than seven times and 2.1% at any time.

The mean frequency of consumption of animal source of vit A was 2.2 in Middle Guinea and 3.6 in High Guinea. The mean frequency of consumption of animal and plant source of vit A (weighted by the source) was respectively 3.81 and 5.23. The main difference in animal vitamin A source seems to be a more frequent consumption of fresh fish in High Guinea.

Illness related indicators are paradoxically better in Middle Guinea where xerophthalmia prevalence is higher.

Vitamin A deficiency seems to be marginal in those populations and a biological assessment should be performed before definitive conclusions.

### VITAMIN A DEFICIENCY IN KENYA

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Vitamin A deficiency one of the most tragic micronutrient deficiencies which affects about 10 million children clinically and 50 million subclinically is the most preventable cause of irreversible blindness. It causes blindness to 350 000 children each year of whom 60% die within one year of becoming blind. Prior to this survey the extent magnitude nor the geographic distribution of vitamin A deficiency in Kenya was known. Vitamin A deficiency was assessed among 6425 preschool children (3298 boys and 3127 girls) aged 6-72 months in 27 clusters randomly selected from 14 districts representative of the country. The deficiency was assessed both clinically through the assessment of clinical signs and biochemically using High Pressure Liquid Chromatography (HPLC). The results indicate that the mean serum retinol was  $0.84 \text{ mmol/l} \pm 0.58 \text{ SD}$  (all children pooled). The mean serum retinol by sex was  $0.82 \pm 0.51 \text{ SD}$  and  $0.87 \pm 0.65 \text{ SD}$  ( $p=0.005$ ) for boys and girls respectively. 8.2 percent of the children were severely vitamin A deficient (< 0.35 mmol/l) and 35.3 percent had marginal vitamin A deficiency (< 0.70 mmol/l). Clinical examination results also show that 15 children (0.2%) had Bitot's spots (X1B), 5 children (0.1%) had conjunctival xerosis (X1A), 53 children (0.8%) had corneal xerosis (X2) and 3 children (0.05%) had corneal scars (XS). This survey the first national micronutrients survey in Kenya demonstrates that regardless of the assessment method used vitamin A deficiency is a significant public health problem in Kenya which requires urgent attention. Geographically the results show that the problem is prevalent in Kwale Mombasa Kitui Baringo Kisumu Kisumu Bungoma Gansa and Mandera. Appropriate well planned interventions need to be targeted to these areas and the at risk groups.

### VITAMIN A DEFICIENCY PREVALENCE SURVEY IN NICARAGUA GE Navas, M Zelaya, A Noguera, Ministry of Health, Managua Nicaragua

The national nutrition survey of 1966 revealed a vitamin A deficiency which did not reach levels of public health significance according to then-current criteria. 11% of children with serum retinol levels below 20mcg/dl. For the next 28 years, Nicaragua suffered earthquake, war, and hurricanes with constant declines in income and nutritional status. In order to assess the current vitamin A situation and plan appropriate control programs a vitamin A deficiency prevalence survey was conducted in a national sample of 1791 children 12-60 mos of age, stratified by major population groups. Managua, other urban and rural areas. Vitamin A status was evaluated by serum retinol concentration (HPLC) and dietary intake as measured by 24 hr recall. Socio-economic factors and recent morbidity were also evaluated.

Overall prevalence of low serum retinol levels was 29%, affecting age groups, sexes and geographic areas equally with higher prevalence in lowest socioeconomic strata. Seven in ten children were found to consume less than 70% of daily recommendations (400 RE). Consumption of vitamin A containing foods and fat were not significantly related to serum retinol status though recent illness especially fever was.

The government of Nicaragua has begun an emergency supplementation effort aimed at preschool age children and is exploring sugar fortification as a long-term control measure.

VITAMIN A STATUS IN THREE AGE GROUPS OF A VENEZUELAN POPULATION Solano Rodríguez L, Peña E, Portillo Z, Yepez C E, Sutil de N R, Del Real S, Marquez M, Diaz N y Rodriguez de M L. Unidad de Investigaciones en Nutrición, Universidad de Carabobo, Fundación Cavendes, Apartado Postal 3458 El Trigo 2002 A, Valencia, Venezuela

Due to the lack of information on the nutritional situation of vitamin A in the Venezuelan population three different age groups were studied: 75 pre-schoolers, 423 schoolers and 99 elderly of low socio-economic income from a Venezuelan city. Serum retinol was measured by High efficiency liquid chromatography and dietary evaluation was determined by 24 hour recall and food frequency questionnaires. The preschoolers group had serum retinol values of  $51 \pm 16.9 \mu\text{g/dL}$  with a 16.5% of them in marginal situation ( $20-30 \mu\text{g/dL}$ ) and 61% showed inadequate intake ( $< 75\%$  of adequacy). Serum retinol values for schoolers were  $47.8 \pm 19.3 \mu\text{g/dL}$  with 20.7% of the children in deficient levels and 10.6% in marginal conditions while 66.6% showed inadequate intake ( $< 75\%$  of adequacy). The elderly population showed mean serum retinol values of  $81.94 \pm 54.6 \mu\text{g/dL}$  but 4.04% of them were deficient and 8.1% were in marginal situation. From this group 68 had dietary assessment finding that 80.8% had a vitamin A intake lower than 400  $\mu\text{g ER}$  ( $< 75\%$  of adequacy). These results are indicative of the derangement of the nutritional status of vitamin A in high risk groups of the Venezuelan population, a situation that is first time reported in our country. Studies on larger groups are necessary in order to have a national diagnosis. A study of 500 pre-schoolers is now being conducted in this Unit. Venezuelan nutritional surveillance system should include the coverage of this nutrient specially when fortification programs of pre-cooked corn flour are now being introduced. (Supported by Codech Universidad de Carabobo, Fundacite Carabobo y Fundación Cavendes)

**Vitamin A Status in Yaqui Indian School Children in Northwest Mexico** ME Valencia, H Astazarán, L González, J Esparza, A Cervera y P Zazueta. Dirección de Nutrición, Centro de Investigación en Alimentación y Desarrollo, A.C. Apdo. Postal 1735, Hermosillo Sonora México 83200

A nutritional survey of 300 school age children (6-10 years) distributed in 26 rural communities was conducted on the Yaqui Indian communities enclaved by one of the most important agricultural valleys in Mexico. Preschoolers were not included due to a previous Vitamin A supplement distribution program. Vitamin A status was determined by retinol and carotenoid serum levels according to (IVACG 1982). For the analysis of serum retinol and carotenoids the communities were classified by size divided into small ( $< 350$ ), medium (750-1200) and large ( $> 4000$ ) inhabitants. Vitamin A intake was assessed in a subsample of the same school age children ( $n=98$ ) by means of a 24 h recall questionnaire with the aid of the mother or the person in charge of meal preparation. Serum retinol distribution showed that 6.3% ( $n=19$ ) of the children were below  $10 \mu\text{g/dl}$  and 40% ( $n=120$ ) were in the range of  $10-20 \mu\text{g/dl}$ . Furthermore significant differences ( $p<0.01$ ) were found between the small and large communities (mean  $\pm$  SEM:  $19.2 \pm 0.8 \mu\text{g/dl}$  and  $22.9 \pm 0.7 \mu\text{g/dl}$ ) respectively. Serum carotenoid levels were significantly higher in large than in small and medium communities (mean  $\pm$  SEM:  $78.1 \pm 2.5$  versus  $65.2 \pm 3.6 \mu\text{g/dl}$  and  $64.4 \pm 3.4 \mu\text{g/dl}$ ) for small and medium respectively. There were no clinical signs of xerophthalmia in the population. The basic food staples were wheat flour, tortillas, pinto beans, corn tortillas, some animal products but in relative small quantities and scarce sources of fresh vegetables. The mean vitamin A consumption was  $244 \pm 29 \mu\text{g RE}$  which represented 34.9% of the US RDA's. The results in this study indicate that almost half of the children were below  $20 \mu\text{g/dl}$  and more than 5% were below  $10 \mu\text{g/dl}$ . According to these findings and using WHO criteria for preschool children this would be a region in which vitamin A could be considered as a public health problem. Probably the younger children of this tribe would have reflected the same vitamin A status of the older group studied, if vitamin A supplement program had not been administered.

PREVALENCE AND RISK FACTORS FOR LOW VITAMIN A IN PERUVIAN CHILDREN Segura L, Cordero L, Benavente L, Marin C, Lescano A, Contreras S, Gilman J, AB PRISMA, Lima, Peru

Before the following information was obtained Vitamin A population status in our country was known only for reduced areas. Therefore Peru was assigned to different country categories of Vitamin A deficiency and information to design appropriate interventions was not available. This study provides the Vitamin A status for a significant part of Peru.

During 1992-93 venous blood specimens were collected in a full representative sample from children less than four years of age. These children were from three socioeconomic strata of Lima: the Capital City which has 32% of the country's population ( $N=225$ ) and from two other cities located in the coast ( $N=94$ ) and the highlands ( $N=74$ ). Samples were transported and stored in the dark and at  $-20^\circ\text{C}$ . Retinol was measured by High Performance Liquid Chromatography (HPLC). The prevalence of serum retinol less than  $20 \mu\text{g/dl}$  (Low Serum Retinol -LSR-) was 3.7% and 24% for the high, middle and low Lima strata and 21% and 24% for the coast and highland cities respectively. In the low strata of Lima bivariate analysis conducted on socioeconomic factors (SEF) and mother and children health information demonstrated significant association with electricity in the home, absence of pre-natal care and stunting. In adjusting the effect of these variables by multivariate analysis stunting and low SEF had odds ratios equal to 2.1 and 1.88 respectively ( $p<0.001$ ). Conclusions: Stunting and low socioeconomic factors are strongly associated with LSR in Lima, Peru. This association gives clues to possible intervention designs and confirms the need to explore the relation between linear growth and Vitamin A.

IMPACT OF CHANGES IN VITAMIN A STATUS ON RESPONSE TO IRON SUPPLEMENTATION IN INFANTS  
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An iron (Fe) supplementation study was carried out in a semi urban region near Peshawar Pakistan which coincided with the summer season when there is an increased intake of fruit and vegetables. 300 infants (average age 13.7 mo) were randomly allocated to receive either 15 mg Fe as ferrous sulphate drops or a placebo orally on a daily basis for 12 weeks. Following supplementation an inverse correlation between plasma retinol and  $\alpha$ 1 antichymotrypsin (ACT) was observed in the Fe supplemented group ( $r=0.42$ ,  $P<0.000$ ) which was not seen in the placebo group (NS).

Further investigation revealed that at baseline there was also a weak correlation between retinol and ACT ( $r=0.19$ ,  $P<0.002$ ). IgA ( $r=0.20$ ,  $P<0.002$ ), IgM ( $r=0.21$ ,  $P<0.001$ ) and IgG ( $r=0.19$ ,  $P<0.01$ ) for all subjects. During the course of the supplementation an improvement in vitamin A status took place in that the plasma retinol increased from  $0.66\pm 0.01$  to  $0.78\pm 0.03$   $\mu\text{mol/l}$  (mean $\pm$ SE) and lutein (an inert marker of vegetable intake) also increased from  $0.102\pm 0.02$  to  $0.218\pm 0.01$   $\mu\text{mol/l}$  (mean $\pm$ SE).

On the basis of these observations we postulate that the improved vitamin A status in the control group reduced the level of residual infection so that retinol no longer correlated with markers of acute phase (ACT) or immune function (IgA, IgG and IgM) in the placebo group. However in the Fe supplemented group the stress imposed by the extra Fe worsened the immune status of those with the poorest retinol concentrations thus increasing the slope of the relationship between retinol and markers of acute phase (ACT) ( $r=0.42$ ,  $P<0.000$ ) and between retinol and the first immunoglobulin to react to antigenic stimulation namely IgM ( $r=0.27$ ,  $P<0.002$ ).

We believe that these data are evidence for the deleterious effects of Fe supplementation in infants constantly exposed to infection but these adverse effects can be reduced by improved vitamin A status.

RELATIONSHIP BETWEEN SERUM VITAMIN A AND IRON STATUS IN ADOLESCENT SCHOOL GIRLS IN DHAKA CITY  
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The relationship between serum vitamin A (retinol) and biochemical indices of iron nutrition was investigated in 225 adolescent girls aged between 12-15 years from four girls schools of Dhaka city, Bangladesh. Eleven per cent of the participants had low levels of serum vitamin A ( $<1.05$   $\mu\text{mol/L}$ ). Twenty two per cent were found to be anaemic (Hb  $<120$  g/L), 15% had subnormal serum iron ( $<7.16$   $\mu\text{mol/L}$ ) and about 25% were iron deficient judged by serum transferrin saturation (TS  $<15\%$ ). Girls in the highest serum retinol group had significantly higher levels of haemoglobin, PCV, MCHC and serum iron. There were significant positive correlations between serum vitamin A and haemoglobin ( $r=0.24$ ,  $p<0.001$ ), PCV ( $r=0.18$ ,  $p<0.01$ ), serum iron ( $r=0.20$ ,  $p<0.01$ ) and TS ( $r=0.18$ ,  $p<0.01$ ). Multiple regression analysis revealed that for 1  $\mu\text{mol/L}$  change in serum vitamin A concentration there was a change of 10.1 g/L haemoglobin, 3.34  $\mu\text{mol/L}$  serum iron and 5.8% TS. The data indicate that there is a relationship between serum vitamin A and biochemical measures of iron nutrition in adolescent girls without overt clinical deficiencies.

## Experiences with Vitamin A Fortification of Foods

## Poster Presentations

EFFECT OF HEAT TREATMENT OF BETA-CAROTENE ADDED TO SOYBEAN COOKING OIL IN RATS AND HUMANS  
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Previous studies in our laboratory showed the possibility to use soybean refined oil as vitamin A carrier. Its the objective of this study was to investigate the nutritive value in rats and the absorption in humans of synthetic beta-carotene added to soybean oil. The evaluation of bioavailability of beta carotene in rats was measured through levels of total vitamin A in plasma and liver. Thirty wistar rats were divided in five groups. Three groups received one of the following balanced basal diet including beta carotene fortified soybean oil with 2, 4 and 8 EqR/g of diet. The other 2 groups received 4 EqR of beta-carotene fortified soybean oil/g of diet after heat treatment at 100°C and 170°C respectively. Absorption of beta-carotene from carotene fortified soybean oil was measured in 16 healthy adults. Each subject served as his own control. They ate rice cooked with 45 mg beta-carotene fortified soybean oil or fortified oil added after cooking of the rice. Plasma sample were obtained on days 0, 1, 2, 7 and 11. In rats liver vitamin A value of synthetic beta-carotene added to soybean oil diet when heated at 100°C kept a level similar to the 4 EqR control group and liver vitamin A value of beta-carotene fortified soybean oil group was reduced by 50% after heating of the oil at 170°C. In men the values of the area under the curve were  $2.05 \pm 0.99$  (mean  $\pm$  SEM) and  $2.27 \pm 1.66$   $\mu\text{mol/l/h}$  ( $p > 0.05$ ) and the peak rise values were  $0.90 \pm 0.31$  and  $0.90 \pm 0.67$   $\mu\text{mol/l}$  ( $p > 0.05$ ) for the group receiving fortified soybean oil added during cooking and after cooking respectively. The results indicate refined soybean oil as a useful beta-carotene fortification carrier.

FORTIFICATION OF SUGAR WITH VITAMIN A IN HONDURAS: PROGRESS, PROBLEMS AND LESSONS LEARNED  
 Vilma Estrada, Anne Swindale and Jose O. Mora  
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The implementation process for sugar fortification with vitamin A in Honduras is described, including problems encountered, lessons learned and approaches to sustainable solutions. Dietary and biochemical assessments in 1965 and 1987 revealed that vitamin A deficiency (VAD) was a serious problem in Honduras. Sugar fortification legislation passed in 1976 was not regularly implemented for many years, law enforcement failed and an effective monitoring system was not developed. In the early 1990s, awareness of the VAD problem and its functional implications generated stronger government commitment. In 1992 the government initiated negotiations with the sugar industry that eventually led to reactivation of fortification and USAID began to support efforts to address VAD through technical and financial assistance. By 1995, fortification was implemented regularly with high coverage more than 90% of the projected demand of sugar for direct consumption was fortified at the industry level, compared with only 13% in 1994 and even less in previous years. Monitoring of fortification at the consumer level is important because sugar for industrial use is not fortified, leakages of fortified and unfortified sugar occur and imports of unfortified sugar are permitted. The government has instituted household level monitoring of fortification levels at low cost through intersectoral collaboration in the gathering of sugar samples.

**ASSESSMENT OF VITAMIN A IN FORTIFIED SUGAR -- SIMPLIFIED** J.C. Arraya, W Canelas, Food and Nutrition Unit, National Secretariat of Health, Oruro, Bolivia

The elimination of Vitamin A deficiency in young children and pregnant women in the poor and barren Altiplano of Bolivia is a challenge we are addressing by fortifying sugar -- the one food product everyone eats at least minimally in this inhospitable region -- with vitamin A. We are conducting a social marketing test market that includes monthly monitoring of sugar throughout the distribution chain to stores and into the home. Using health workers posted throughout the region to buy and collect the sugar, we will analyze it in the lab in La Paz, giving us monthly trends of the deterioration rate of the retinol palmitate and the consumption of vitamin A by the target audience, namely children under 5 and pregnant women. Since this system is not intended to identify EXACT levels of vitamin A in the sugar, it is simple, quick, and less costly than most. The test market has started in October, 18th 1995 in the department of Oruro.

**β-CAROTENE CONTENT IN FORTIFIED BRAZILIAN PASTA AND EVALUATION OF ANALYTICAL METHODOLOGY** Maricilda R Pereira, J Amaya-Farfan and D Rodriguez-Amaya, Dept of Food Planning & Nutrition, School of Food Engineering, State University of Campinas, CP 6121, Campinas 13081-970, SP, Brazil

Brazilian pasta manufacturers have been fortifying these long shelf life cereal products with β-carotene on a voluntary basis for over a year. Since the success of fortification programs depend on the reliable monitoring of the enriching nutrient, we report on the evaluation of this Brazilian attempt with pasta. From three extraction procedures tested that of Livingston (1986) coupled with open-column separation of β-carotene from oxidized products (Rodriguez-Amaya *et al* 1976) was chosen for the raw pasta. Forty-one sample lots encompassing six manufacturers, seven different spaghetti brands in the time span of six months, all claiming vitamin A values between 200 and 400 RE/100g, were assayed. The total carotenoid content varied from 0.9 to 5.9 μg/g of pasta with a mean of 3.2 μg/g and β-carotene levels ranging from not detected to 3.8 (mean of 1.8 μg/g). If the total carotenoid content were used for calculating the vitamin A values, all of the samples would fall within or above the range stated in the label. However, when the degradation products were separated from β-carotene, the vitamin A values fell to 0 to 630 RE/100g, thus bringing eleven of the samples below the minimum and nine above the maximum stated on the labels.

## Poster Presentations

## Biologic Significance of Vitamin A Deficiency Infection

**IMPACT OF VITAMIN A SUPPLEMENTATION ON MORBIDITY PATTERN IN RURAL PRESCHOOL CHILDREN** K. N. Agarwal, D. K. Agarwal, C. M. Pandey, Departments Pediatrics, University College of Medical Sciences, GTBH, Delhi, Institute of Medical Sciences, Banaras Hindu University, Varanasi and Department of Biostatistics, SGGGIMS, Lucknow, India

To study the impact of vitamin A supplementation on morbidity, a randomized double blind trial was conducted in rural children 1-6 y of age in Varanasi District of Uttar Pradesh, state of India. The morbidity information was collected fortnightly during January 1991 to February 1992. 1514 children received vitamin A+E (supplemented) and 1200 received vitamin E as control. Vitamin A supplementation for one year resulted in 10% reduction of overall morbidity (P/0.001). The relative risk was 1.7 times in control group as compared to vitamin A supplemented group. The higher morbidity risk was mainly due to infections like intestinal (1.8 times), upper respiratory (1.9 times), acute otitis media and pneumonia (1.4 times). The supplementation of vitamin A was more effective in reducing morbidities in 13-84 m of age and in immunized children. Vitamin A supplementation reduced morbidities in children of large families, lower parental education and those consuming well or pond water.

In a hospital based study in 59 diarrhoea and 59 acute respiratory infection (ARI) children, vitamin A levels were lower as compared to age & matched control. In these patients in association with malnutrition the values were further reduced.

The measurements of height, weight and midarm circumference did not differ in vitamin A supplemented and non-supplemented groups.

**VITAMIN A SUPPLEMENTATION IN THE FIRST 6 MONTHS OF LIFE: DOES IT REDUCE DIARRHOEA AND ARI MORBIDITY?** SE Arifeen and AH Baqui, Urban MCH FP Extension Project, International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh

This study presents results of a double blind, randomized, placebo controlled trial evaluating the efficacy of vitamin A supplementation in early infancy using EPI contacts. The Government of Bangladesh has a policy of supplementing young infants with vitamin A when they come for their EPI shots. This study was designed to provide key information in the review of these policy recommendations. The study was conducted in an urban poor population in Bangladesh. One hundred and twenty-one infants received 3 doses of vitamin A and another 125 were given a placebo at the three recommended EPI contacts. Since the dose of vitamin A was reduced during the study, about 68% of the infants in the supplemented group received 3 doses of 25,000 IU each, about 7% received 3 doses of 50,000 IU each and the remaining received at least one dose of 50,000 and 25,000 IU. The infants were visited every fortnight to collect information on occurrence of diarrhoea and respiratory infections since the last visit. Univariate and standard multivariate analysis revealed no significant morbidity differences between the supplemented and placebo groups. However, there was a consistent pattern of slightly higher, but non-significant, risk of diarrhoea and respiratory infections among the supplemented infants. The possibility of increased risk of morbidity is consistent with recent findings from other parts of the world and have significant policy implications.

**EFFECT OF VITAMIN A SUPPLEMENTATION ON THE INCIDENCE OF COUGH, DIARRHEA, AND FEVER** Herrera MG, Fawzi WW, Nestel P, El Amin A, Mohamed KA Harvard School of Public Health, Boston, Massachusetts, USA and Ministry of Health, Sudan

Vitamin A supplementation has been shown to reduce mortality in most, but not all randomized trials reported to date. Contrary to expectations, supplementation was without effect on the incidence of symptoms of infection even in a trial that achieved a reduction in mortality of > 50%. These paradoxical results, together with the dramatic protective effect of vitamin A against mortality observed among measles patients, suggest that vitamin A may modulate only the severity of infections or that its effects are disease specific. We have analyzed further the data obtained in the randomized, placebo controlled trial conducted in the Sudan to investigate the possible effects of vitamin A supplements on mortality and morbidity. Preschool children free of symptoms of vitamin A deficiency were assigned either to a treatment group that received 200,000 IU of vitamin A every six months or to a placebo group. At baseline and at each of three follow up visits data were obtained on the presence of cough, fever, and diarrhea during the week prior to the survey. The actions taken by the family concerning the illness of the child were also recorded. Dietary intake of vitamin A was monitored at each follow up visit. Supplementation significantly increased the incidence of cough but was without effect on diarrhea and fever. Dietary intake of vitamin A was associated with increased cough but was inversely associated with the incidence of diarrhea and with the incidence of cough and fever occurring together. The effect of supplementation on the incidence of symptoms over time will be presented, as will the results of multivariate analyses used to identify other factors that predicted morbidity or modified the effects of vitamin A supplementation.

## Dietary Interventions

## Poster Presentations

**PREVENTION OF VITAMIN-A DEFICIENCY THROUGH HORTICULTURAL INTERVENTIONS** Indira Chakravarty Director Professor & Dean All India Institute of Hygiene and Public Health, Calcutta India

The present work is being conducted to assess the impact of horticultural interventions to combat vitamin-A deficiency in some of the most drought prone areas. For situation analysis baseline data was generated with regards to clinical signs of deficiencies dietary intake pattern rapid rural appraisals dietary intake as per IVACG method knowledge-aptitude and practices for vitamin A (VA). Results showed very high prevalence of VA deficiency eg Bitot's spot-2.8% conjunctival xerosis 6.4% and night blindness 15.3% due to deficit intake of VA (423 ug) among 77.1 families for low consumption of green leafy vegetables and fruit as well as their low availability and also poor knowledge aptitude and practices with regard to VA rich foods. Based on the baseline survey intervention was given by distributing seeds seedlings fertilizers manure etc to the surveyed households and also theoretical and field training on horticultural aspects nutrition health and environmental education bio-intensive gardening socio-economic issues and women's role. Central nurseries were also built. All inputs were provided twice due to seasonal requirements eg rainy season and winter months. During impact evaluation (being initiated recently) it is being observed that there is a significant improvement in the consumption of green leafy vegetables.

**A STUDY ON DIFFERENT INTERVENTIONS TO IMPROVE THE VITAMIN A NUTRITURE AMONG PRE-SCHOOL CHILDREN** RP Devadas, U Chandrasekhar and S Premakumari, Food Science and Nutrition Department, Avinashilingam Deemed University, Coimbatore India

The main objective of this study was to find out the operational feasibility of incorporating Vitamin A in the diets of pre-school children and to evolve low cost locally feasible intervention technology to improve the Vitamin A nutriture of pre-school children. In order to carry out this study 100 pre-schools (Anganwadies) under the National Integrated Child Development Scheme in Coimbatore city were selected and divided into four groups (A, B, C and D) of 25 anganwadies each. Children in Group A were supplemented with Amaranthus (30g/child/day) while children in Group B were given nutrition education along with Amaranthus supplementation. In group B anganwadies, the supervisors were motivated to raise Vitamin A rich gardens as part of nutrition education and the harvest of Vitamin A rich foods were included in their daily meals. Children in Group C were administered oral dose of Vitamin A (200000 IU/child/6months) while those in Group D were given nutrition education along with the administration of oral dose of Vitamin A. The supplementation was carried out for a period of one year and the impact was evaluated in terms of their anthropometric measurements clinical and biochemical pictures (blood hemoglobin and serum Vitamin A levels) of the children and knowledge, attitude and practices of the mothers. Among the different interventions tested, supplementation of Amaranthus along with nutrition education (group B) resulted in best outcomes, followed by groups A, D and C. The study also created awareness among the anganwadi workers, supervisors, mothers and children on the importance of Vitamin A in their daily diets and enthused the mothers to raise Vitamin A gardens in their houses.

PROMOTION OF VITAMIN A RICH FOOD SOURCES THROUGH AN INTEGRATED IEC PROGRAM Martha Burdick de Piedrasanta, Edmundo Alvarez Jeffrey Brown International Eye Foundation (IEF), Guatemala City, GUATEMALA and IEF, Bethesda MD USA

The IEF has been implementing an integrated nutrition IEC program in vitamin A deficient, rural communities in Guatemala's northern Department of Alta Verapaz since 1990. Baseline data indicated that over 21% of children, ages one to six years exhibited serum retinol levels of less than 20 mcg/dl.

Education activities promoting consumption of vitamin A-rich foods have been directed at mothers with young children and have consisted of cooking demonstrations, group discussions, puppet shows, theater, stories and radio spots. Similarly the promotion of home gardens and the development of revolving-seed funds have been linked to these efforts to increase the availability of vitamin A rich vegetables.

Recent evaluations, which included focus groups with mothers, and community leaders, have shown that families highly value nutrition education activities. Coverage of radio spots is almost universal. Similarly, changes have been measured in the knowledge levels of mothers in regards to foods rich in vitamin A. A June 1995 knowledge, practice and coverage (KPC) survey showed over 84% of mothers knew two or more sources of vitamin A, an increase of 12% from a similar 1993-94 survey. Currently over 83% of mothers feed their children, ages five months and older, vitamin A-rich foods at least twice weekly.

These findings suggest that IEC activities play an important role in increasing the consumption of vitamin A-rich foods.

A simple method to evaluate whether consumption of vitamin A rich foods increased and if, so which foods results from nutrition intervention activities in two regions of Niger Burger SE, Oumarou A Brah F, Abdou O, Sabou D, Magagi A, Berge P & Baker SK. Helen Keller International 90 Washington St. New York NY 10006

A Helen Keller International (HKI) project was implemented to assist the Government of Niger and other organizations to reduce vitamin A deficiency among preschool children and women in Maradi and Tahoua. A Vitamin A Committee composed of members from key governmental organizations, HKI and USAID was established to ensure that intervention activities were consistent with national policy as well as region specific resources, conditions and needs.

In both Maradi and Tahoua existing resources made it feasible to distribute vitamin A capsules and to promote greater consumption of vitamin A rich foods through health facilities. The existence of an Academy for Educational Development Nutrition Communication project in the region of Tahoua provided an opportunity to promote vitamin A rich foods using radio and village theater. In one district in Tahoua, the Food and Agricultural Organization implemented a small scale intensive home gardening project.

A previously validated Food Frequency Method (FFM) was used to collect quantitative data in January 1994 and again in 1995. In each region, 15 villages were selected by proportional to population size random start sampling. About 1400 mothers of preschool children (12-71 months old) were randomly selected from the census list kept by the village chief. Only 1 child was selected per mother. Mothers were asked to recall how many days the selected child consumed 31 different food items in the previous 7 days and whether their child received a vitamin A capsule (VAC) in the last six months.

The frequency of intake of vitamin A-rich foods in 1994 was significantly greater in Tahoua ( $p < 0.05$ ). In Tahoua the frequency of intake of vitamin A rich foods increased significantly from 1994 to 1995 particularly among animal sources ( $p < 0.05$ ). These findings could be explained by a significant increase in the frequency of intake of liver, butter, fish and mango ( $p < 0.05$ ). Liver, dark green leafy vegetables (DGLV) and mango and orange squash were actively promoted. In Maradi on the other hand, the frequency of intake of vitamin A-rich foods actually declined significantly. Almost no children consumed foods fortified with vitamin A in either region. Those children who received a VAC in the last six months ate vitamin A rich foods significantly more frequently than children who did not receive a VAC ( $p < 0.05$ ).

The increase in consumption of vitamin A rich foods is consistent with the expected response to the intervention activities implemented in Tahoua. Alternative explanations for the response in Tahoua such as increased rainfall, decreased food prices or increased economic status are being analyzed in further depth. Tahoua is poorer and more drought-prone than Maradi. Reasons for the decreased consumption in Maradi will be explored in further depth.

PREVALENCE OF VITAMIN A DEFICIENCY AMONG ADOLESCENT GIRLS IN COLOMBO SRI LANKA AND THE IMPACT OF NUTRITION EDUCATION ON VITAMIN A STATUS

P Lanerolle, I M S Atukorala, G de Silva and S Samarasinghe. Department of Biochemistry, Faculty of Medicine, University of Colombo, Sri Lanka and Office of the School Medical Officers, Ministry of Health, Sri Lanka.

There have been no studies on vitamin A status of adolescent girls in Sri Lanka. A study was carried out to assess the prevalence of vitamin A deficiency and anaemia among adolescent girls from low socioeconomic groups and to assess the impact of nutrition education on vitamin A status. One hundred and seventy-two adolescent girls (mean age  $15.3 \pm 1.1$  years) from five schools in Colombo where the majority of girls attending were from low socioeconomic groups were selected. Their vitamin A status was assessed by measuring serum vitamin A concentration and by conjunctival impression cytology. The haemoglobin concentration was also measured. Their knowledge on nutrition was assessed and an interviewer-administered questionnaire was used to determine the frequency of consumption of vitamin A-rich foods. All subjects were then given nutrition education and reassessed after a period of 10 weeks. Serum vitamin A levels less than  $20 \mu\text{g/dl}$  were noted in 10.5% of the subjects. Abnormal conjunctival impressions were noted in 7.9% of subjects. Anaemia (haemoglobin  $< 120 \text{g/L}$ ) was present in 17.7% subjects. There was a significant ( $p < 0.001$ ) improvement in knowledge on nutrition after educational intervention. Further, there was an increase in consumption of common vitamin A-rich foods. A significant increase in serum vitamin A ( $p < 0.01$ ) and haemoglobin ( $p < 0.01$ ) concentration was also noted. Our results show that education was effective in bringing about a desirable change in food habits and an improvement in vitamin A status.

Community Based rehabilitation of the malnourished children  
Using cereal-Vegetable fortified flours

By Dolhne Busolo (Kenya)

As a result of the indigenous vegetable based product development research work we developed various weaning food recipes using dehydrated vegetables. This was an intervention strategy to harness the high levels of the micronutrient present in the vegetables to process into a palatable flour to alleviate rampant malnutrition levels (30-40%) identified in the Keno project sites in Bungoma district. The area is mainly sugarcane growing zone with minimum vegetable production. Traditionally children are weaned on the cereal porridge with no fortification neither are they given vegetables in the diets hence the high incidence of morbidity, anaemia and protein energy malnutrition in the vulnerable group. A women's group composed of community health workers formed good lineage for the intervention. The work is undertaken collaboratively with Kengo playing the facilitation role while the group undertakes the implementation by dehydration of the vegetables, milling them in composting them with cereals and legumes and selling them at clinics to the under-fives, lactating and pregnant mothers in conjunction with the ministry of health. The vegetables are also preserved as source of vitamins and sold/eaten during drought (6-8 months). There is significant reduction in the levels of malnutrition to  $< 10\%$  and there are more households producing and consuming vegetable for their home consumption which can be translated into income saving on vegetable expenditure at household level. Some income though not yet quantified has been realized from the sale of vegetables. The project model is being documented for replication by UNDP in other areas with similar problems.

**INDIGENOUS FOODS A SOURCE OF VITAMIN A IN HONDURAS** E.V. Lopez and D. Chunchilla Direction of Food and Nutrition Ministry of Health and PAHO/INCAP Representative Honduras Central America

The 1987 Food Consumption Survey found that 73% of Honduran families consume less than half of the recommended amount of Vitamin A. The Food Composition Tables for Latin and Central America show that many of the indigenous Central American vegetables are an important source of provitamin A or carotenes.

Dark green leaves and bright yellow or orange vegetables are common in rural areas in Honduras and can be easily grown or gathered. Therefore a simple methodology was developed to identify such foods to promote their production and consumption.

Foods containing the highest amounts of B-carotenes were selected from the Food Composition Tables. A group of women from the community were selected to cook twelve recipes. These recipes required traditional cooking utensils and methods of preparation. The food was tasted by women and children in the rural areas. The sensory evaluation revealed a high level of acceptability and a low cost in nine of the twelve recipes.

The preparations were submitted to chemical analysis to determine their carotene content comparing their values before and after cooking. The recipes analyzed were: rice with pumpkin (*Cucurbita pepo*), deep orange sweet potato (*Ipomoea batata*) croquettes, scrambled eggs with chaya leaves (*Cnidoscolus chayamansa*), carrot (*Daucus carota*) croquettes, mashed sweet potato, pumpkin dessert, mango (*Mangifera indica*) dessert, scrambled eggs with radish leaves (*Raphanistrum sativus*) and fried bananas (*Musa paradisiaca*).

It was found that cooking some vegetables reduces the carotene content while cooking others increases the level.

Rice with pumpkin, deep orange sweet potato croquettes, pumpkin dessert and mango dessert were found to reduce carotene levels.

The recipes which increased carotene levels were carrot croquettes, scrambled eggs with radish leaves, scrambled eggs with chaya leaves and fried bananas.

The results suggest that carotene levels increase when vegetables are cooked with oil, but more research is necessary to confirm such a conclusion.

However, the amount of change in the vitamin level is minimal, therefore the study concludes that most of the foods studied, whether cooked or not and cooked with oil or not, provide an excellent source of vitamin A.

**SERUM RETINOL LEVELS IN PRESCHOOL CHILDREN IN SOUTHERN GHANA AND THE EFFECT OF COOKING ON THE  $\beta$  CAROTENE LEVELS OF COMMONLY USED LEAFY VEGETABLES** E. E. K. Takyi and E. Harrison Noguchi Memorial Institute for medical Research University of Ghana P O Box 25 Legon Ghana

Our previous study of the serum retinol levels of 263 village inhabitants (aged 3-60yr) in southern Ghana indicated that even though that community was not a vitamin A deficient community when based on WHO classification. Deficient levels of retinol ( $< 10 \mu\text{g/dL}$ ) were found only in the 3-5 year old age group. This group therefore formed the focus group in our present studies in which preschool children in 4 communities were monitored to determine if their retinol levels conform to WHO specification. Of the 162 cohorts examined 3.7% had Deficient serum retinol, 16.7% had Low level ( $10- < 20 \mu\text{g/dL}$ ), 78.40% had Adequate level ( $20-50 \mu\text{g/dL}$ ) while 1.23% had High level ( $> 50 \mu\text{g/dL}$ ) indicating non endemicity of VAD.

In order to assess the effects of some traditional cooking practices on  $\beta$ -carotene levels of some commonly used leafy vegetables, fresh/raw vegetables were boiled for varying periods and the  $\beta$ -carotene levels determined using HPLC. Interesting results were obtained in that while there were significant reduction in the  $\beta$ -carotene level of some of the boiled leafy vegetables, relative to raw/fresh tissue values, significant increases were seen in others, while there was no significant change in others.

These results could at least partially explain reports in the literature that there was no increase in the serum retinol in some subjects fed vegetables. This underlines the importance of studying individual vegetables rather than extrapolating results from one vegetable to another. This paper also seeks to highlight the fact that special attention must be paid to cooking practices to ensure maximum benefit from  $\beta$  carotene in the vegetables. Furthermore, there is an urgent need to promote the consumption of those vegetables whose  $\beta$  carotene levels increase on boiling since these might have higher bioavailability. This must be done through nutritional education.

The implications of these findings in the control of micronutrient deficiency at the National level in Ghana will be discussed.

**PROVITA HOUSEHOLD DISTRIBUTION OF GREEN, YELLOW AND ORANGE PLANTS AS A MODEL SYSTEM FOR SUSTAINABLE PROVITAMIN A ENRICHMENT PROJECTS: LONGITUDINAL RESPONSE OF BIOCHEMICAL BIOMARKERS** Jesus Bulux, Marylena Arta, Hector Gamero, Noel W. Solomons, Center for Studies of Sensory Impairment, Aging and Metabolism (CeSIAM), Dr. Rodolfo Robles, Eye and Ear Hospital, Guatemala City 01011, GUATEMALA

Natural food sources of provitamin A from among the green, yellow and orange edible plants have been projected as the basis for a sustainable public health solution to vitamin A deficiency. Our PROVITA project in the rural Santa Rosa Province of Guatemala was dedicated in part to determining whether and if so how *quilete* (*Solanum americanum*), a leafy herb, sweet potatoes (*Ipomoea batata*) and carrots (*Daucus carota*) would be prepared and consumed and distributed in the meals of the various generations of the poor rural homes. Previously (IVACG XVI 1994 p 88) we presented the results on changes of consumption behavior in a full distribution hamlet (I), an eligible-child only distribution hamlet (II) and a control hamlet (III). At baseline (August 1991) and at closure (August 1992) the primary ( $\alpha$  and  $\beta$  carotene and retinol) and secondary markers ( $\alpha$  and  $\gamma$  tocopherol, cryptoxanthin and lycopene) were determined in plasma samples. A total of 205 blood samples were collected at baseline and 226 at closure, within which there were 120 within subject longitudinal pairs. The paired results were used for analysis of the across site intervention effect (Table). Overall plasma retinol at baseline was  $29 \pm 11 \mu\text{g/dL}$ . No nutritional effect of the intervention could be ascertained as no differential retinol response was detected. This could be due to poor bioconversion from intrinsic factors of plants or extrinsic factors of the background hosts: vitamin A nutrition. The changes in carotenoids and xanthophylls, however, provide biomarker confirmation of the differential intake of plant sources, as indicated by the behavioral data taken in an interview format.

**MEDIAN 1 YEAR CHANGES IN PLASMA ANALYTES WITH PAIRED SAMPLES**

	hamlet I	hamlet II	hamlet III
retinol ( $\mu\text{g/dl}$ )	0.2	2.3	5.3
$\alpha$ carotene ( $\mu\text{g/L}$ )	16.5	20.0	8.5
$\beta$ carotene ( $\mu\text{g/L}$ )	41.0	42.0	22.5
$\alpha$ tocopherol (mg/L)	2.1	3.2	1.5
$\gamma$ tocopherol (mg/L)	0.21	0.06	0.13
cryptoxanthin ( $\mu\text{g/L}$ )	21.0	29.0	0.0
lycopene ( $\mu\text{g/L}$ )	8.0	16.0	8.0

The PROVITA Project was supported by USAID through the International Eye Foundation (Bethesda). The assays were performed courtesy of Dr. W. Schup of Hoffmann-La Roche, Basel, Switzerland.

**PROVITAMIN A CONTENT OF VEGETABLES IS LOWER THAN REPORTED IN FOOD TABLES** PJM Hulshof<sup>1)</sup>, X. Chao<sup>2)</sup>, P. van de Bovenkamp<sup>1)</sup>, CE West<sup>1,3)</sup> 1) Department of Human Nutrition Wageningen Agricultural University, the Netherlands; 2) Department of Nutrition and Food Hygiene, Shenyang Medical College, Shenyang, P.R. China; and 3) Rollins School of Public Health of Emory University, Atlanta, GA, USA.

Many of the data on the provitamin A content of foods incorporated in food composition tables have been obtained by methods which do not exclude non provitamin A carotenoids. Therefore we have measured the provitamin A content of a number of selected vegetables: sweet potatoes and mangos from Indonesia by HPLC; Water spinach (*Ipomoea aquatica* n=8), spinach (*Amaranthus viridis* n=8), cassava leaves (*Manihot utulissima* n=8), papaya leaves (*Carica papaya* n=9), sweet shoot leaves (*Sauropus androgynus* n=4), jointfir spinach (*Gnetum gnetum* n=2), sweet potato (*Ipomoea batatas* n=22) and mango (*Mangifera indica* n=11) were sampled from different markets and fields in the Bogor district of West Java, Indonesia. Carotenoids in the edible portions were extracted using tetrahydrofuran and analyzed on a reversed phase Vydac 218 TP 54 column. Babyfood from Nutricia Nederland BV Zoetermeer, the Netherlands comprising carrots, peas, low fat milk and Gnetum was used as a control food and analyzed in each run. Individual carotenoids were monitored at 450 nm, identified by retention time and spectral analysis and quantified from calibration plots. Retinol equivalents (RE) in the samples were calculated as  $1/6 \beta$  carotene ( $\mu\text{g}$ ) +  $1/12 \alpha$  carotene ( $\mu\text{g}$ ) +  $1/12 \text{ cis } \beta$ -carotene ( $\mu\text{g}$ ). Recovery studies showed recoveries (mean  $\pm$  sd) of  $94.8 \pm 2.0\%$  and  $97.4 \pm 1.9\%$  for  $\alpha$  and  $\beta$  carotene respectively. Within and between run coefficients of variation for  $\alpha$  carotene were 6.1% and 5.8% and for  $\beta$  carotene 7.6% and 6.1% respectively. Provitamin A content (mean and 95% confidence interval) per 100 g edible portion was 492 [335-649] RE for water spinach, 640 [500-780] RE for spinach, 1776 [1402-2150] RE for cassava leaves, 992 [668-1316] RE for papaya leaves, 1889 [1147-2631] RE for sweet shoot leaves, 289 [0-1167] RE for jointfir spinach, 6 [0-15] RE for sweet potato and 250 [42-458] RE for mango. The provitamin A content of waterspinach, spinach, papaya leaves, jointfir spinach and sweet potato were lower compared to Indonesian food tables. It can be concluded that the method gave reliable results as indicated by the high recovery and low variation. As suggested earlier (West & Poortvliet VITAL/USAID 1993), previously published values in food tables on the provitamin A content of vegetables are too high.

CAROTENE RICH FRUITS AND VEGETABLES THEIR CAPACITY TO IMPROVE VITAMIN A STATUS OF CHILDREN IN WEST JAVA A COMPARISON WITH DIETARY RETINOL SOURCES

S. de Pee C E West Muhilal J G A J Hautvast Department of Human Nutrition Wageningen Agricultural University The Netherlands and Nutrition Research and Development Centre Bogor Indonesia

Our recent study in West Java showed no improvement of vitamin A status of breastfeeding women after consumption of an additional daily portion of dark green leafy vegetables for 12 weeks (The Lancet 1995 346 75 81) This contradicts the assumption that increased consumption of dark green leafy vegetables will improve vitamin A status After thorough review of the literature (Eur J Clin Nutr in press) we conclude that evidence for the assumption is weak Because of the urgent need for more information about the effect of carotene rich foods such as dark green leafy vegetables and fruits on vitamin A status we have carried out another intervention study in West Java in the period July - October 1995

We have examined the change of vitamin A status of children after consumption of different sources of vitamin A Average age of the children was 10 y and their haemoglobin concentration <120 g/L or haematocrit <36 L/L Per school children were randomly allocated to four groups (n=53 60) All children received 2 meals per day for 6 d per week over a 9 wk period The meals were almost identical except for vitamin A content Per day they received White group <80 RE (retinol equivalents) Green group 650 RE from dark green leafy vegetables Purple group 650 RE from fruits Red group 650 RE from retinol rich foods The differences in meals were realized by exchanging foods with high vitamin A content for foods with low vitamin A content for example mango vs starfruit Duplicate portions were collected for food composition analysis For each child meal consumption was observed every day and consumption of foods other than those provided by the study was recorded once every week Stools were examined for parasite eggs and cysts Parameters measured at baseline and follow up included weight height haemoglobin concentration haematocrit white blood cell counts and serum concentrations of retinol carotenoids ferritin transferrin receptor and albumin

The study was approved by the Medical Ethics committee of the Indonesian Ministry of Health and the Indonesian Institute of Science Caretakers gave written informed consent before the start of the study After the study all participants received a megadose vitamin A (200 000 IU) medication to treat parasitic infestation and if necessary iron pills

## Poster Presentations

## Biologic Significance of Vitamin A Deficiency Growth and Inflammation

THE MECHANISM OF INFLAMMATION INDUCED HYPORETINEMIA  
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In children with measles or other infections the concentration of plasma retinol (ROH) decreases to  $\leq 0.70 \mu\text{mol/L}$  ( $20 \mu\text{g/dL}$ ) this hyporetinemia is most severe during the acute phase of infection and is associated with a poor prognosis However neither the cause of infection induced hyporetinemia nor its relationship to vitamin A status are well understood As an approach to understanding the mechanism of hyporetinemia during infection inflammation was induced with lipopolysaccharide (LPS from *Pseudomonas aeruginosa*) in vitamin A sufficient rats, the kinetics of plasma ROH and the mechanism of hyporetinemia were examined Following LPS ( $50 \mu\text{g}$  administered intraperitoneally per  $100 \text{ g}$  body weight) plasma ROH decreased significantly 10 h after dosing reaching the lowest level by 24 h and remaining so up to 72 h In a second experiment the reduction in plasma ROH was accompanied by a significant reduction in plasma retinol binding protein (RBP) by 12 h and transthyretin (TTR) by 24 h after LPS At 24 h liver and kidney RBP and TTR protein concentrations were also significantly reduced but tissue ROH concentrations were normal In the liver the relative abundance of RBP mRNA (messenger RNA) was reduced in LPS vs control rats ( $0.48 \pm 0.11$   $n = 5$  pairs  $p < 0.01$ ) Paradoxically the relative abundance of kidney RBP mRNA did not change ( $1.22 \pm 0.18$   $n = 5$   $p > 0.10$ ) We also assessed the relative abundance of cellular retinol binding protein mRNA (a cytosolic protein involved in the intracellular transport and metabolism of ROH) and found it not affected in the liver ( $0.91 \pm 0.10$   $p > 0.10$ ) nor in the kidney ( $1.30 \pm 0.16$ ,  $p > 0.10$ ) We infer from this model that hyporetinemia during infection results from a reduced hepatic synthesis and secretion of retinol RBP Moreover these data imply that plasma ROH is a poor indicator of vitamin A status during infection We recommend that an independent measure of inflammation such as plasma C reactive protein be used to aid in the interpretation of plasma retinol levels in populations where infections are prevalent

CORD BLOOD RETINOL AND RETINOL-BINDING PROTEIN IN HEALTHY PRETERM AND TERM NEONATES AND NEONATES WITH RISK FOR BRONCHOPULMONARY DYSPLASIA R Valdés-Ramos MSc, JA Cardona-Perez MD, B Topete-Lezama BSc, YO Pacheco BSc, C Meza-Camacho BSc, E Udaeta-Mora MD

Vitamin A deficiency causes abnormalities in cellular replication affecting the functional and structural integrity of epithelial cells Retinol and retinol binding protein concentrations were evaluated from cord blood in three groups of neonates in order to identify any differences between healthy term (group I  $\geq 37$  weeks) and preterm babies (group II  $\leq 36.6$  weeks) as well as those with a high risk to develop bronchopulmonary dysplasia (group III  $\leq 1500 \text{ g}$ ) This last group was followed-up until 28 days of life when diagnosis was established Group I ( $n=41$ ) had normal retinol and retinol-binding protein concentrations at birth, while group II ( $n=58$ ) had suboptimal retinol ( $< 40 \mu\text{g/dL}$ ) and retinol-binding protein ( $< 3 \text{ mg/dL}$ ) concentrations suggestive of hypovitaminosis in the preterm babies Group III consisted of 17 neonates who required mechanical ventilation during at least their first three days of life and had diagnosis of Bronchopulmonary Dysplasia (BPD) at 28 days Anthropometric and laboratory evaluations were done at birth, 4, 7, 14, 21 and 28 days of life, with previous informed consent of the parents Of the total sample, 3 children developed grade I BPD, 13 had grade II and 1 had grade III Mean gestational age at birth was of  $38.8 \pm 1.8$  weeks, 8/17 were hypotrophic and the rest were normal, while 8/17 were female Mean plasma retinol concentrations ( $\mu\text{g/dL}$ ) were at birth of  $20.7 \pm 6.9$ , at day 4 of  $15.9 \pm 6.0$ , at day 7 of  $21.8 \pm 6.0$ , at day 14 of  $17.4 \pm 6.2$ , at day 21 of  $15.5 \pm 5.7$  and at day 28 of  $14.3 \pm 5.7$  Anthropometric measurements showed a slight increase although they were always below reference values

VITAMIN A AND INTRAUTERINE GROWTH RETARDATION  
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A case-control study examined the association between cord and maternal levels of vitamin A and fetal growth in 356 Brazilian mothers who delivered intrauterine growth retarded (IUGR) babies and 356 mothers who delivered appropriate for gestational age (AGA) babies

Newborns were classified as being IUGR according to the Lubchenco classification Gestational age of the newborns was evaluated by the Capurro method Vitamin A was measured by high performance liquid chromatography (HPLC)

Thirty three point one percent (33.1%) IUGR babies and 14.6% AGA babies had levels of vitamin A  $\leq 0.70 \mu\text{mol/l}$  ( $p < 0.001$ ) However maternal levels of vitamin A  $\leq 0.70 \mu\text{mol/l}$  were similar for both IUGR (1.1%) and AGA mothers (1.4%)

The results suggest that vitamin A deficiency was not a problem for the mothers in this population

There are four possible explanations for the lower cord levels of vitamin A in IUGR babies compared to AGA babies inadequate supply poor fetal binding, increased utilisation by the fetus and poor storage by the fetus

The association between cord levels of vitamin A and fetal growth persisted even when other known confounders were taken into account

## Using Ethnographic Methods in Vitamin A Deficiency Research

## Poster Presentations

LOOKING FOR LONG TERM SUSTAINABILITY THE VITAMIN A COMPONENT OF EL SALVADOR'S NUTRITION EDUCATION PROGRAM LY Munoz\* M Griffiths -Dep of nutrition Ministry of Health San Salvador El Salvador The Manoff Group Washington D C USA

El Salvador a country with multiple and severe nutrition problems has undertaken during the past five years a comprehensive program to reach communities particularly those classified as high risk for nutrition and health problems with nutrition services Key among these services is nutrition education The nutrition education program departed from past attempts in that its goals are improvements in practices by families related to use of products in the case of vitamin A the vitamin A fortified sugar and better household practices such as the inclusion of vitamin A rich foods in daily diets particularly diets of young children The basis for the design of the program was a comprehensive qualitative investigation of attitudes perceptions and practices of families across El Salvador This was followed by a draft communication strategy for each component and for the program as a whole The vitamin A component follows the general pattern of others with radio spots and mini programs and interpersonal materials for the use by health and development personnel and material for school children A quantitative baseline done prior program launch indicated some of the challenges 99% of children 6-36 months and 95% and 96% of pregnant and nursing women did not meet their requirement for vitamin A intake 60% of children had multiple illnesses during the two weeks prior to the interview more than half (57%) of mothers could not name a food rich in vitamin A and only one third knew that vitamin A rich foods should be consumed daily by children The presentation will review the materials developed on fortified sugar and vitamin A rich foods and will present initial monitoring information

WHY CHILDREN DON'T EAT THEIR VEGETABLES AN ANTHROPOLOGICAL APPROACH TO VITAMIN A DEFICIENCY IN WEST JAVA INDONESIA L E Carlin Department of Anthropology University of Durham Durham UK

Recent studies of children's vitamin A (VA) status have highlighted the importance of intra household food allocation Research into food habits and VA deficiency has suggested the potential importance of food taboos and other dietary beliefs for specific nutrient deficiencies This biocultural study of VA deficiency in rural West Java examined children's food consumption as a form of behavior subject to household customs food beliefs and also cultural rules for child parent interaction

The study focused on 20 children ages 3 to 10 years with Bitot's spots and/or night blindness and 20 age- and sex matched non VA deficient controls The symptomatic children all showed response to treatment with one or two capsules of 200 000 IU retinol The controls were selected for their above average serum retinol levels (range= 0.77-2.24  $\mu\text{mol/L}$  median=0.86  $\mu\text{mol/L}$ )

Food intake was recorded by trained observers over 4 days VA intake was measured by dietary recall using a preliminary version of the IVACG Simplified Dietary Assessment Household socioeconomic status mother's knowledge (both western and traditional) about food for children and the relationship between children's diet and health were ascertained from interviews with caretakers Participant observation provided contextual data

Results show that while traditional food beliefs do tend to discriminate against the provision of VA rich foods adherence to traditionality does not differentiate mothers of VA deficient children from those of matched controls Dietary profiles demonstrate reduced diversity of nutrient sources and lower frequency of snacking for cases as compared to the controls which largely reflect differences in household wealth Beyond the constraints of budget and beliefs lies the domain of rules for adult child interaction by which adults rarely exert control over children's behavior including eating Consideration of these rules could productively influence the planning of information and education campaigns dedicated to increasing consumption of fruits and vegetables for example by targeting children rather than their parents

DECREASED PREVALENCE OF XEROPHTHALMIA AND IMPROVED NUTRITIONAL STATUS AMONG PRESCHOOLERS FOLLOWING VITAMIN A SUPPLEMENTATION AND NUTRITION EDUCATION INTERVENTIONS IN THE PHILIPPINES Tuason Lopez C Villate E, Klamn R (HKI Philippines) Burger S (HKI NY USA) Gorstein J (University of Michigan) Mendoza O (University of the Philippines College of Public Health)

The aim of the Vitamin A Expansion (VITEX) project was to improve the vitamin A status and growth of children in three provinces of the Philippines. Municipalities were randomly assigned to receive nutrition interventions through the following channels: (i) radio alone (ii) radio and comic books (iii) radio comic books and mothers classes and (iv) radio comic books mothers classes and home counseling. Nutrition education included promotion of healthy breastfeeding and infant feeding practices and promotion of vitamin A from food or capsules. Distribution of vitamin A capsules (VACs) was originally targeted to underweight children identified during the annual village based weighing (Operation *Timbang*). In 1993 however the Philippine government expanded VAC distribution to cover all one to five year old children every six months.

A baseline survey was conducted from May to July 1991 and an endline survey was conducted during the same months in 1994. Over 11 000 preschool children from 120 randomly selected villages were examined for signs of xerophthalmia and measured for anthropometry. Mothers were interviewed about their knowledge about vitamin A whether their child had received a VAC in the last six months their participation in Operation *Timbang* and whether their child exhibited nightblindness.

In surveyed areas VAC coverage increased from 6.8% at baseline to 85.9% at endline. The prevalence of night blindness among children 24 to 59 months old declined significantly to just around the World Health Organization (WHO) criteria of 1.0% in all four intervention groups. The prevalence of moderate and severe underweight (based on the Philippines weight for age reference values) declined significantly among children six to 23 months old in all but the intervention group that received radio messages alone.

Logistic regression analyses were conducted to identify factors that influenced VAC receipt after controlling for age gender intervention group and nutritional status. Children were significantly more likely to have received a VAC if their mothers: (i) participated in Operation *Timbang* (odds ratio (OR) = 2.2) (ii) correctly identified  $\geq 3$  dietary sources of vitamin A (OR = 1.2) or (iii) knew the benefits of vitamin A (OR = 1.34).

#### EFFICIENT VITAMIN A SUPPLY THROUGH INHALATION HK Biesalski Department of Biological Chemistry and Nutrition University of Hohenheim Fruwirthstr 12 D 70593 Stuttgart Germany

Vitamin A deficiency is associated with alterations of the respiratory epithelium like loss of cilia increased number of mucous secreting cells and squamous metaplasia. The consequence of these alterations is an impairment of the self cleaning activity of the epithelium resulting in increased occurrence of respiratory diseases especially observed in vitamin A deficient children. Indeed vitamin A supplementation usually lowers the risk for respiratory infections. Yet in presence of diarrhoe severe protein deficiency or with insufficient daily supply the vitamin is not approaching the target tissues. Insufficient amounts and the respiratory mucosa can not maintain its normal appearance. To overcome this problem we developed an inhalative application. Vitamin A deficient male SD rats (n = 12 ca 200 g) and healthy male volunteers (n = 16 normal nutritional state) were investigated. Following inhalation (1 000 IU) the rat respiratory epithelium showed an uptake of retinyl esters (7.5  $\mu\text{g/g}$  dry solid) and the tissue revealed a normal appearance (light and electron microscopy). In contrast control vitamin A-deficient rats (without inhalation n = 8) exhibited the typical morphological alteration of the respiratory epithelium (mucous metaplasia). In human volunteers the inhalative application of retinyl esters (3000 IU) resulted in a maximum concentration of plasma retinyl esters within 30 minutes (before inhalation  $44.7 \pm 13.1$  ng/ml after inhalation  $189.3 \pm 67.1$  ng/ml). Inhalative application was not accompanied with any side effects or complaints. This might yield as a promising novel method to facilitate organ specific targeting of vitamin A.

#### CONTRIBUTING TO REDUCE THE NUTRITIONAL PROBLEM AND VITAMIN A DEFICIENCY IN WESTERN GUATEMALA

Victor Calderon M D M P H Chief Vitamin A Program  
Project HOPE Quetzaltenango Guatemala

The overall project goal is to reduce the infant morbidity and mortality due to vitamin A deficiency. This goal is to be reached through cost-effectiveness community sustainable interventions in three departments of Guatemala highland.

The principal objectives are: To increase in 60% the supplement of Vitamin A in children between 6 to 72 and 50% of women after delivery. Training 90% of MOH (Ministry of Health) and MOA (Ministry of Agriculture) staff and community volunteers on nutrition vitamin A and home gardens in the target areas. Target families (40%) will grow vitamin A rich vegetables in their own garden and 50% of families with children 6 to 72 months with gardens will consume vegetables at least twice a week.

In 1991 HOPE completed serum retinol surveys in 3000 children under 5 age showing vitamin A deficiency in 20% of them. (In Guatemala more than 5% of the population with low levels of retinol is a Public Health problem).

A project main characteristic is to work predominantly in rural communities of difficult access as well as to strengthen institutional coordination as a strategy of extension and increase of coverage through the involvement of the Ministries of Health (MOH) and Agriculture (MOA) and NGOs (Non Governmental Organizations). These institutions receive technical and financial assistance vitamin A capsules seeds and educational materials as well as they serve as multipliers for community groups.

Another important component is the sustainability intervention of community groups. To avoid members of the community to expect receiving all benefits free cost recovery activities were initiated i.e. selling of vegetable seeds by health promoters and agricultural representatives. In coordination with The General Direction of Livestock a model farm (with chickens rabbits vegetables greenhouses etc.) was implemented. Farms like this model are being established in the target communities to improve the family nutritional status.

Project's investigations are based on community work and on the information that families did not consume vitamin A rich food. The program target population is 178 000 children under 6 age and 43 000 women after delivery. The program performs two evaluation one at the mid term and at the end of the project.

Effects of vitamin A supplements and deworming with albendazole on the vitamin A status of Indonesian children as assessed by a simplified modified relative dose response (MRDR) test. S.A. Tanumihardjo, D Permasih Muherdiyantiningsih, E Rustan Muhilal, D Karyadi and J A Olson Dept of Biochem & Biophys Iowa State Univ Ames IA USA Nutrition Research & Development Ctr Bogor West Java Indonesia

The modified relative dose response (MRDR) test for assessing vitamin A status has been used in several surveys. In order to simplify field procedures two standard doses of 3.4 dihydroretinyl acetate (5.3  $\mu\text{mol}$  and 8.8  $\mu\text{mol}$ ) were administered to Indonesian children (n = 34) at a one month interval. While the higher dose elicited a higher response within an individual (P = 0.0002) neither dose response was related to body weight (P < 0.39). In another group of children (n = 83) the MRDR test was administered (0.35  $\mu\text{mol/kg}$  body weight) and two blood samples were drawn per child between 3 and 7 h after dosing. The MRDR ratio increased with time and plateaued between 5 and 7 h. Using this information the MRDR test was used in Indonesian children (n = 309 0.6-6.6 y) known to be infected with *Ascaris lumbricoides*. Six different treatments including a 210  $\mu\text{mol}$  vitamin A supplement and a 400 mg dose of albendazole were randomly administered together or at different times during a 1 mo period. Vitamin A supplementation was most important in improving vitamin A status (P < 0.0001) whereas deworming (P = 0.370) and the statistical interaction between deworming and vitamin A (P = 0.752) were not. Serum retinol values marginally improved (P = 0.051) in two groups that received vitamin A and albendazole but not in the third group that received vitamin A only. The MRDR test proved a better discriminator of the treatment effects on vitamin A status than did changes in serum retinol values. (Supported by the Thrasher Research Fund 2808-2 SmithKline Beecham Pharmaceuticals and USDA CRP 94-37200-0490).

**PREVENTION AND CURE OF XEROPHTHALMIA AMONG CHILDREN IN SOUTHERN INDIA ARE IMPROVED BY A WEEKLY LOW DOSE VITAMIN A SUPPLEMENT** RC Milton<sup>1</sup> BA Underwood<sup>2</sup> L Rahmathullah<sup>3</sup> and RD Thulasiraj<sup>4</sup> <sup>1</sup>The EMMES Corporation Potomac MD USA <sup>2</sup>WHO Geneva Switzerland <sup>3</sup>Aravind Children's Hospital and <sup>4</sup>Eye Hospital Madurai India

**Background** We have previously reported that small weekly doses of vitamin A similar to the RDA when provided to children in an area of vitamin A deficiency and undernutrition were effective in reducing mortality. We now report on the impact of this supplementation on prevention and cure of xerophthalmia. **Methods** We conducted a randomized controlled masked clinical trial for one year in southern India among 15 419 children age 6-60 months who received weekly doses from community health volunteers of either 8333 IU (2500 µg) vitamin A and 20 mg vitamin E (treated group) or vitamin E alone (control group). Xerophthalmia status was ascertained at baseline and at 6 and 12 months follow up by trained field workers and verified by a medical officer. Children with signs of xerophthalmia were treated with 200 000 IU vitamin A and remained in the study. **Results** Prevalence of xerophthalmia at baseline was 11%. **Prevention** Among children without xerophthalmia at baseline the risk of developing xerophthalmia in the treated group at 6 mos follow up was less than half of that in the control group (RR = 0.44). Similar reduction was seen among children without xerophthalmia at mid term with follow up to the end of the year. **Cure** Among children with xerophthalmia at baseline the risk of remaining xerophthalmic in the treated group was 3/4 of that in the control group (RR = 0.74). **Conclusion** Regular supplementation by vitamin A at a level potentially attainable from foods in an area of vitamin A deficiency and undernutrition contributes substantially to prevention of xerophthalmia (incidence was reduced by one half) and to cure of xerophthalmia (prevalent cases were reduced by one fourth) even when all cases also received an initial large therapeutic dose.

## Vitamin A Status Methodology

## Poster Presentations

**A TEST OF HKI METHODS OF QUALITATIVE ASSESSMENT OF VITAMIN A DEFICIENCY PROBLEMS IN A RURAL AREA NEAR PUNE INDIA** V. Persson, T. Greiner and IP Bhagwat. Unit for International Child Health Uppsala University, Sweden and BAIF Development Research Foundation Pune India.

We studied whether the methods described in two HKI manuals (Conducting a Qualitative Assessment of Vitamin A Deficiency and How to Use the HKI Food Frequency Method to Assess Community Risk of Vitamin A Deficiency) could be used effectively by a Nutritionist (VP) and a MD (IPB) neither with particular expertise in vitamin A. The goal was to determine within a few weeks whether VAD was likely to be a public health problem in Kasurdi, a village of 3000 in an arid rural area 35 km from Pune (annual rain fall 300 mm) where BAIF have health and agriculture projects. If so we hoped that the study would also suggest measures that might be taken to improve the situation.

First, existing reports were reviewed, 13 key informants interviewed, 4 group discussions held and local markets and shops surveyed. Second about 1/3 of the households in the village known to have children aged 1-5 were sampled beginning at random point, yielding 70 children whose eyes were examined for signs of VAD. The HKI Food Frequency method was applied to one sibling from each family chosen randomly for a sample size of 53.

In the state of Maharashtra Bitot's spots (XI B) was found in 0.4% of preschool children in 1990. In Kasurdi XN was seen fairly regularly by some health workers in young children and women of reproductive age especially in the poorer groups. For many good food sources are either not affordable or not available much of the year. Colostrum is discarded but breast feeding continues for over one year in most cases and over two years fairly often.

In all of the studied groups the mean frequency of consumption of vitamin A was below 4 per week for animal sources and 5 per week for weighted sources (animal + 1/6 plant). This was below the cut off points of 4 and 6 respectively suggested by HKI.

However we question HKI's decision to exclude breast milk and cow milk from the calculations. Breast milk is one of the most important sources of vitamin A in the infant's diet even in the second year, supplying on the order of 160 RE at 13-24 months (Newman 1993). Thus it should be included.

In this study 13 of the 15 children aged 1-2 years were still breast fed, 12 of these three times a day or more. Cow milk was very commonly given to children in this area but the concentration of vitamin A left in the milk as served needs further investigation. The inclusion of breast milk and cow milk raised the overall mean of weighted sources from 3.3 to 8.2.

Both fat and protein scores were adequate for all groups. VAC coverage for the past six months for children 1-3.5 years of age was 63%. XI B was seen in the eyes of three of the 70 children (4.3%).

Both manuals were found to have clear instructions and to be easy to use. The methods fulfilled the objectives of indicating to the NGO involved that VAD is likely to be a problem and providing some ideas for useful interventions which indeed are being planned.

**EVALUATION OF A FOOD FREQUENCY QUESTIONNAIRE TO ESTIMATE VITAMIN A INTAKE IN PRESCHOOL AGE CHILDREN IN INDONESIA** M. Dibley (1), M. Serdula (2), Th. Ninuk SH (3), T. Sadjimin (4). (1) Johns Hopkins University Baltimore, USA, (2) Division of Nutrition Centers for Disease Control Atlanta, USA, (3) Nutrition Academy MOH, Yogyakarta, Indonesia, (4) CEBU Gadjah Mada University Yogyakarta, Indonesia.

Effective and reliable tools are needed to measure dietary vitamin A intake in preschool age children both for research and monitoring dietary interventions. Dietvita aimed to assess the reproducibility and validity of a food frequency questionnaire to measure vitamin A intake in preschool-aged children from a developing country. Dietary intake was assessed in 296 children aged 6 through 47 months at enrollment. Weighed food intakes of each child over a 14 hour period were recorded on 6 occasions during a month and a deuterium oxide method was used to measure average two weekly breastmilk intake in the breast fed children. A 57 item food frequency questionnaire with a one month referent period was developed using IVACG guidelines and was administered at the start and end of each survey period. Nutrient intakes were calculated using the International MmiList database. A food score was calculated for the food frequency data by multiplying the intake frequency by the average portion size by the nutrient density. The items on the food frequency questionnaire accounted for 84% of the vitamin A intake observed in the weighed food intakes. The mean vitamin A intake as measured by the food frequency questionnaire (384 RE/day) was nearly twice as high as that measured by the weighed food intakes (201 RE/day). The Pearson correlation coefficient between initial and final food frequency questionnaires ( $r=0.50$ ) was similar to that reported in other studies. The correlation between food frequency and weighed food intakes was higher for food frequencies administered after compared to before food weighing (<24 months 0.25 vs 0.35 ≥ 24 months 0.17 vs 0.28). The food frequency method evaluated was appropriate to identify major dietary contributors of vitamin A, to detect temporal changes in intake, to identify target groups & possibly to rank individuals by intake. It was not appropriate for measuring absolute intake of vitamin A.

**LUTEIN AS A MARKER OF VEGETABLE INTAKE AND VITAMIN A STATUS** DJ Thurnham CA Northrop Clewes P Paracha and UJ McLoone Human Nutrition Research Group University of Ulster Coleraine Northern Ireland BT52 1SA and Department of Human Nutrition University of Peshawar Peshawar Pakistan

Vegetables and fruits are the major source of vitamin A for the populations of the developing world.  $\beta$  Carotene is the principal pro vitamin A compound in vegetable foods but because the amount of  $\beta$  carotene in blood represents the excess of intake over requirements plasma  $\beta$  carotene itself is not a good marker of vitamin A intake. Lutein however is present in most vegetables in approximately the same amounts as  $\beta$  carotene (Heinonen et al *J Agric Fd Chem* 1989 37 655-659) it is not converted to vitamin A and dietary intake was reported to correlate with plasma concentrations better than either lycopene or  $\beta$  carotene in 80 vitamin A adequate Cambridge (UK) women measured at four times during one year (Scott et al *Brit J Nutr* in press)

We recently measured lutein,  $\beta$  carotene and retinol in plasma from 267 Pakistani infants with a mean age of 13 mo in August 1993 (mean(SE) 0.102(0.015) 0.011(0.006) 0.66(0.014)  $\mu$ mol/l resp). Three months later at the end of the summer season the same analyses (n=207) were done again (0.202(0.008) 0.011(0.002) 0.78(0.019) resp) when all three markers increased (P<0.02 paired t test). However in the case of plasma  $\beta$  carotene the increase was negligible but the proportion of non detectable results fell from 90% to 69% over the 3 mo. At baseline lutein did not correlate with retinol in the girls (r=+0.029) but did in the boys (r=+0.363 P<0.000) in contrast to the follow up data where it correlated in both sexes absolute measurements (boys r=+0.362 P<0.000 girls r=+0.259 P=0.01) and for the differences (boys r=+0.472 P<0.000 girls r=+0.300 P<0.003). There was no correlation between  $\beta$  carotene and retinol at either time or in either sex. The infants were breast fed with some supplementary feeding but we have no information on either. The infants were probably obtaining most dietary vitamin A from breast milk and the increase in plasma retinol in these infants probably reflects the increased availability of vegetables to the mothers during the summer period. We have found lutein in the milk of Pakistani women (unpublished) and the evidence suggests that plasma lutein in the infants reflects increased vegetable intake by the mothers and is also an indirect marker of changes in vitamin A status.

**LINKING A VITAMIN A DEFICIENCY RISK ASSESSMENT QUESTIONNAIRE WITH A SERUM RETINOL VITAMIN A DEFICIENCY PREVALENCE STUDY IN THE REPUBLIC OF THE MARSHALL ISLANDS** NA Palafox C Kjolhede M Gamble J Gittlesohn J Langidrik B Blaner K Briand John Burns School of Medicine University of Hawaii Hawaii USA Ministry of Health and Environment, Majuro Republic of the Marshall Islands (RMI) Johns Hopkins School of Hygiene and Public Health Baltimore MD USA Columbia University Institute of Human Nutrition Columbia NY USA

Clinical evidence of significant malnutrition and vitamin A deficiency (VAD) in children has been present in the RMI for the last ten years. Initial attempts to determine VAD prevalence and to develop a VAD surveillance and prevention project were unsuccessful. This project was undertaken to 1) determine the national and strata specific prevalence of VAD in children ages 1-5 using serum retinol 2) develop a country sensitive risk assessment questionnaire for future population surveillance and individual risk assessment for VAD. The risk assessment tool would also provide insight to possible VAD intervention strategies specific to RMI. Methodology: A stratified single stage cluster sampling technique was utilized to obtain the designated sample of 800 serum retinols. 200 sera were randomly drawn from each of four strata: two urban centers, the outer islands, the people from the radiation affected atolls. The VAD prevalence was determined in each of the strata. The parents of every fifth child was asked a series of 15 questions regarding VAD risk factors in the Marshall Islands. The questionnaires were scored and the results were linked to individual serum retinol levels to assess its sensitivity and specificity as a screening tool for individuals with normal and low levels of serum retinol. Findings: 800 children (ages 1-5) were tested for serum retinol. 55% of children had serum retinol levels less than between 10-20 mcg/dl and 8% had retinol levels less than 10 mcg/dl suggesting significant VAD. The results of the correlation of the risk assessment questionnaire to serum retinol levels will be completed by December 1995. Conclusions: Serum retinol can be utilized with greater precision to determine VAD in areas where health workers are not trained to clinically screen children with VAD. A significant portion of the children of RMI (63%) have serum retinol levels below 20 mcg/dl. The VAD risk assessment questionnaire, validated with serum retinol levels, provides a valuable method to perform surveillance and has established risk factors on which to base interventions in the RMI.

Acknowledgements: UNICEF Suva Fiji; Fergusson Foundation, Kona Hawaii

**A MODIFIED METHOD TO MINIMISE LOSSES OF CAROTENOIDS AND TOCOPHEROLS DURING HPLC ANALYSIS** G Lietz and CJK Henry School of Biological and Molecular Sciences Oxford Brookes University Oxford OX3 0BP UK

HPLC is potentially an excellent method for the separation and quantification of provitamin A carotenoids and their isomers. Prior to the analysis of carotenoids and tocopherols saponification has often been employed as an effective purification step for the removal of chlorophylls, lipids and to release the esterified xanthophylls. However several researchers have found significant losses of xanthophylls after saponification. Furthermore, it has been shown that elevated temperatures and prolonged exposures to alkaline conditions resulted in significant losses of  $\alpha$  tocopherol.

In order to minimise these effects an HPLC method developed by Hart and Scott (1995) has been modified by using *Candida cylindracea* lipase for mild hydrolysis. This microbial lipase from *Candida cylindracea* is supposed to be a non specific lipase (Micaree 1983) and preferentially hydrolyses  $C_{14}$  to  $C_{18}$  saturated and monounsaturated fatty acids (Lae and Lambertsen 1986). As palm oil consists of 44%  $C_{16}$  and 39%  $C_{18:1}$  *Candida cylindracea* seems to be an optimal tool to hydrolyse palm oil. The lipase catalysed hydrolysis of the oil was carried out in a 50ml Quikfit Erlenmeyer flask at 35°C containing *C. cylindracea* preparation (10mg 943 units/mg solid Sigma) 100 mg of palm oil sodium phosphate buffer (pH 7.0 0.08 M 35ml) and Ascorbic acid (50ppm) stirred for 16 h. This method was modified from Rahmatullah et al (1994). The reaction mixture was extracted three times with 20 ml diethyl ether/petroleum ether (2:1 (v/v)). The three extracts were combined and washed three times with 50 ml 10% sodium chloride solution and finally the organic solvent was evaporated to dryness in a rotary evaporator. The residue was redissolved by ultrasonic agitation to a final volume of 5 ml in dichloromethane filtered through a 0.45  $\mu$ m PVDF syringe filter (Whatman) and diluted with the mobile phase to a suitable concentration for HPLC analysis according to Hart and Scott (1995). This modified procedure will form the basis of our presentation.

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**DIFFERENCES IN SERUM RETINOL CONCENTRATIONS IN MOTHER-INFANT PAIRS AT BIRTH BY ETHNIC ORIGIN IN THE NEGEV (SOUTHERN ISRAEL)** R Gorodischer B Sarov E Gazala E Hershkovitz S Edvardson D Sklan and M Katz Dept of Pediatrics and Ob-Gyn Units of Epidemiol and Clin Pharmacol Soroka Medical Center and Faculty of Health Sciences Ben-Gurion Univ Beer-Sheva and Fac of Agric Hebrew Univ Rehovot Israel

**Background:** Subclinical vitamin A deficiency is related to increased morbidity and mortality in infants. Previous studies indicate that the traditional diet of Moslem Bedouins, an important ethnic group in Southern Israel, is low in vitamin A content.

**Methods:** Serum retinol was measured by HPLC in 313 healthy mother-infant pairs at birth following term gestation (>37 weeks) of normal birth weight infants (BW  $\geq$ 2500 gm), 175 Jews and 138 Bedouins.

**Results:** Retinol <20  $\mu$ g/dl was measured in 11% of mothers and in 24% of infants. Cord retinol <20 and <10  $\mu$ g/dl were measured in 17% and 11% of Jewish and 33% and 7% of Bedouin newborns respectively (both p=0.001). As compared to mothers with serum retinol  $\geq$ 20  $\mu$ g/dl a larger % of mothers with serum retinol <20  $\mu$ g/dl gave birth to infants of shorter gestational age (37-38 weeks 26.5 vs 15.2% n.s.) and to lighter infants (birth weight 2500-2990 gm 42 vs 24% p<0.01). In contrast to infants with birth weight  $\geq$ 3000 gm a larger % of infants with birth weight 2500-2990 gm had cord serum retinol <20  $\mu$ g/dl (35 vs 20% p<0.006). Neither maternal nor infant serum retinol was related to socioeconomic indices.

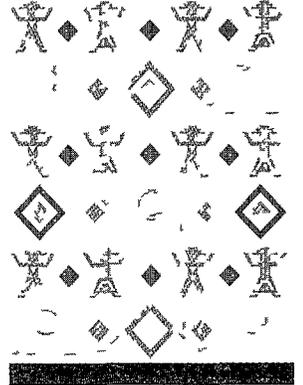
**Conclusion:** Low serum retinol was found prevalent in mothers and newborns in Southern Israel and particularly in Bedouin infants. Low serum retinol in maternal and cord blood was associated with a lower birth weight in this population of apparently normal infants.

PREVALENCE OF SUBCLINICAL VITAMIN A DEFICIENCY AMONG YOUNG INFANTS IN BANGLADESH  
M A Wahed, J O Alvarez, M M Rahman, M Hossain, F Jahan, D Mahalanabis, and D Habte  
International Centre for Diarrhoeal Disease Research Bangladesh (ICDDR,B), and Dhaka Shishu Hospital, Bangladesh and University of Alabama at Birmingham, Al 35294-0008

In Bangladesh the high prevalence of clinically evident vitamin A deficiency in children under 5 years has been well documented however little is known about the vitamin A status of infants. The relative dose response (RDR) test was carried out in 85 healthy infants (5.9±2.3 months) coming to the International Centre for Diarrhoeal Disease Research Bangladesh (ICDDR,B) or Dhaka Shishu Hospital for routine immunization. Mean serum retinol [R] was  $0.66 \pm 0.3 \mu\text{mol/L}$  and mean RDR value was  $29.8 \pm 22.1$ . Fifty-seven percent (57%) of the infants had serum [R] values under  $0.70 \mu\text{mol/L}$  and 18% under  $0.35 \mu\text{mol/L}$ . Sixty-four percent (64%) of the infants had abnormal RDR values ( $\geq 20$ ) indicating low liver reserves of vitamin A. RDR values showed a negative correlation with weight for age. The RDR test showed a high sensitivity detecting 93% of infants with  $0.355 \leq [R] \leq 0.695 \mu\text{mol/L}$  as abnormal. These results indicate that there is a high prevalence of subclinical vitamin A deficiency in Bangladeshi infants. Supported in part by U.S. AID grants DPE-5986-A-00-1009-00 and DHR-5600-G-00-0084-0.



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