The Nutrition Foundation, Inc.

ANNUAL REPORT OF

COOPERATIVE AGREEMENT

DAN-5115-A-00-7114-00

1 October 1992 to 30 September 1993

Table of Contents

Cooperative Agreement No. DAN-5115-A-00-7114-00
Annual Report, Fiscal Year 1993
1 October 1992 to 30 September 1993

Executive Summary

Fiscal year 1993 marked the sixth year of a cooperative agreement between The Nutrition Foundation, Inc. and the Office of Nutrition, Bureau for Research and Development, U.S. Agency for International Development (AID). In FY93 this cooperative agreement provided funding for three international nutrition programs: International Vitamin A Consultative Group (IVACG), International Nutritional Anemia Consultative Group (INACG), and International Nutrition Planners Forum (INPF).

The cooperative agreement, originally a five-year agreement, was extended by AID to cover the sixth year. No funds were provided in FY93 for a continuation of a fourth program, International Nutrition Network Exchange. The Joint Micronutrient Consultative Group, with combined representation from IVACG, INACG, and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD), was active during FY93.

The activities of these programs are in three primary areas: providing a forum for new ideas through sponsoring international meetings, preparing and distributing state-of-the-art technical references, and fostering international liaison. These activities bring together individuals interested in improving nutritional status and strengthening food and nutrition institutions and personnel, particularly in developing countries.

The secretariat at the Nutrition Foundation provides managerial, administrative, and logistic support for each program. Because IVACG, INACG, and INPF are not formal membership organizations, the secretariat also provides essential continuity from year to year. International experts donate their time to determine priorities for the groups and to provide technical expertise through steering committees and task forces. These committees and task forces include individuals from donor organizations, those involved with intervention programs, and scientific authorities.

There were three major achievements in FY93, one in each of the primary program activity areas. Each achievement represents a new effort by the Nutrition Foundation to improve on past successes and to strike out on new paths to aid in controlling micronutrient malnutrition.

First, the Nutrition Foundation organized a very successful XV IVACG Meeting in Arusha, Tanzania. Nearly 300 scientists, program planners, and policy officials came from over 50 countries to participate in discussions of how to implement comprehensive programs to reduce vitamin A deficiency. One new aspect of the XV IVACG Meeting was a session devoted to other micronutrients, e.g., iron and iodine. The Nutrition Foundation also produced a meeting summary that is being distributed widely.

The second major achievement was INACG's publication of *Iron EDTA for Food Fortification*. This monograph is the end product of an INACG task force that began work in FY91. In addition to the monograph, INACG submitted a toxicology monograph on sodium iron EDTA to the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and was pleased that JECFA granted provisional approval for the use of the compound in food fortification programs. This represents the first time an international body or national regulatory agency has approved the use of this versatile source of iron.

The third major achievement highlights the fostering of international liaison. Through the Joint Micronutrient Consultative Group (JMCG), the Nutrition Foundation organized a Joint Micronutrient Mission to the Philippines. The JMCG looks at integrated approaches to micronutrient malnutrition. The mission to the Philippines was a unique effort to test the feasibility of using a micronutrient team approach to explore options for effective integrated strategies.

In addition to these achievements, the Nutrition Foundation produced two other important publications -- *Nutrition Communications in Vitamin A Programs: A Resource Book* and *A Brief Guide to Current Methods of Assessing Vitamin A Status*.

A primary function of the Nutrition Foundation is the distribution of the information generated by IVACG, INACG, and INPF. The Nutrition Foundation responded to more information and publications requests this year than in any previous year. The Nutrition Foundation also strengthened liaison efforts with other groups working to eliminate micronutrient deficiencies.

All necessary financial reports were filed on time. The total federal share for expenditures for fiscal year 1993 were $533,736.73.

The Nutrition Foundation exceeded cost-sharing (matching) requirements required by amendment no. 7 of the cooperative agreement. In that amendment, the Nutrition Foundation agreed to provide $1,400,000 to be distributed among the programs. At the end of fiscal year 1993, the Nutrition Foundation's non-federal cost-sharing totaled $1,791,972.66, exceeding the agreed cost-sharing amount by $391,972.66.

Throughout fiscal year 1993, the Nutrition Foundation continued to work closely with the AID project officers for the Office of Nutrition. Their collaboration and that of the Director of the Office of Nutrition, Mr. Richard Seifman, was essential to the success of the Nutrition Foundation's activities.

International Vitamin A Consultative Group (IVACG)

Introduction

The Nutrition Foundation, Inc. first received financial support as the secretariat for IVACG in 1975. Funding continued through the following years. The IVACG Secretariat receives its current support through a cooperative agreement between the Nutrition Foundation and the AID Office of Nutrition. The cooperative agreement began 1 October 1987 and was to end 30 September 1992. Through extensions, funding continued through the sixth year of the agreement which is covered in this annual report.

The mission of IVACG is to guide international activities for reducing vitamin A deficiency in the world. In order to carry out this mission, IVACG sponsors international meetings and scientific reviews. It convenes task forces to analyze and make recommendations related to the causes, treatment, and prevention of vitamin A deficiency in developing countries. Task force reports provide guidelines and strategies to assess the prevalence of vitamin A deficiency; refine assessment techniques; and develop, monitor, and evaluate intervention programs. The examination of these issues is important to the establishment of public policy and action programs.

IVACG guidelines and strategies are generally disseminated through IVACG's state-of-the-art monograph series. These monographs, along with IVACG meeting reports, achieve worldwide circulation through channels of the United Nations agencies, AID and other international aid agencies, nongovernmental organizations, educational institutions, and private industry, and through direct correspondence with professionals working in developing countries.

IVACG also provides information regarding country and donor program activities to interested individuals. Through its international meetings, IVACG provides a forum to foster the interchange of ideas, the presentation of new research findings and survey data, and discussion of action programs.

The IVACG Steering Committee recommends priorities for the organization's programs and publications. (A list of steering committee members is Appendix 1 of this report.) The IVACG Secretariat provides managerial, administrative, and logistic support to the IVACG Steering Committee and to IVACG task forces. In carrying out these functions, the secretariat collaborates closely with the AID Office of Nutrition. Dr. Frances R. Davidson, Senior Nutrition Advisor at the Office of Nutrition, serves as secretary of IVACG.

XVI IVACG Meeting

At the close of FY93, plans are underway for the XVI IVACG Meeting. Earlier in the year, colleagues at the Institute of Nutrition at Mahidol University (INMU) recommended Thailand as the site for the XVI IVACG Meeting, and the IVACG Steering Committee agreed with this suggestion. Dr. Abraham Horwitz, IVACG Chair, received an official invitation to IVACG from Dr. Kraisid Tontisirin. After consultation with Dr. Davidson, Dr. Horwitz responded affirmatively to the invitation. The secretariat communicated with Dr. Kraisid and other INMU colleagues about the meeting, formation of a local committee in Thailand, meeting dates, meeting site, and a November 1993 pre-meeting site visit by Ms. Aomari. The meeting will be held 24-28 October 1994 in Chiang Rai.

The secretariat consulted the IVACG Steering Committee about potential meeting themes. Once the theme is determined, the call for abstracts will be circulated during Q1FY94. The steering committee will be involved in decisions about the meeting when they meet in November 1993. Other arrangements for the meeting will continue throughout FY94.

XV IVACG Meeting

The XV IVACG Meeting, "Toward Comprehensive Programs to Reduce Vitamin A Deficiency," took place 8-12 March 1993 in Arusha, Tanzania. Representatives from 51 countries were among the 293 policy makers, programmers, and scientists in health, nutrition, biochemistry, agriculture, horticulture, and development who participated in the XV IVACG Meeting. The five-day program included 77 oral presentations, 51 poster presentations, and four video presentations related to the meeting theme, and to research concerning progress in changing dietary behaviors related to vitamin A, newer methodologies for assessing subclinical vitamin A deficiency, consequences for human health and development of vitamin A deficiency, and functions of vitamin A (see Appendix 2).

Participants had the opportunity to review and order materials from 17 exhibits, including an exhibit by the Nutrition Foundation that included many IVACG publications. The project manager presented a report from the Nutrition Foundation, Inc. during the final session of the XV IVACG Meeting.

Five IVACG Secretariat staff members managed all on-site arrangements for the XV IVACG Meeting (8-12 March); a meeting of the IVACG Steering Committee (evenings of 9 and 10 March); a meeting of the INPF Steering Committee (7 March); a meeting of the INACG Steering Committee (12 March); and three post-meeting study tours (13 March). Additionally the secretariat facilitated arrangements for events held by the University of Iowa (7 March) and Johns Hopkins University (10 March).

The IVACG Secretariat coordinated study tours with World Vision, Tanzania; UNICEF, Tanzania; the National Horticultural Research Centre and Training Institute at Tengeru, Tanzania; and the local organizing committee in Tanzania. These trips provided an opportunity for participants to learn more about conditions related to vitamin A deficiency in Tanzania; and to view child survival, agriculture, horticulture, sanitation, community action, and education efforts aimed to improve these conditions.

Much advance preparation was necessary for this meeting. During the first and second quarters, the IVACG Administrative Committee (i.e., Dr. Horwitz, Dr. Davidson, Dr. Underwood, Dr. Harris, and Ms. Aomari) communicated and met to work out program details, confirm rapporteurs, determine funding for participants, and agree on the meetings to be held in conjunction with the XV IVACG Meeting.

In consultation with the IVACG Steering Committee, the meeting program was finalized, and the secretariat issued invitations and confirmations to all presenters and rapporteurs. Many of the presentations were selected from abstracts submitted in the second half of FY92. Dr. Keith P. West, Jr., Dr. Paul Arthur, and Mr. Claver Temalilwa agreed to serve as meeting rapporteurs.

The secretariat prepared a general invitation brochure for the meeting and distributed it to more than 1080 individuals and organizations working outside Tanzania (Appendix 3). In response to the invitations, the secretariat received and acknowledged numerous inquiries and requests for financial assistance. These requests were reviewed with the IVACG Administrative Committee. With pre-approval of the Office of Nutrition, IVACG funds from Cooperative Agreement No. DAN-5115-A-00-7114-00 were used to support the travel and per diem of 21 meeting participants and Nutrition Foundation staff members.

A fund-raising letter was forwarded to 11 international and 17 domestic agencies, nongovernmental organizations, industries, and foundations. Contributions for the meeting were received from Australian International Development Assistance Bureau; Bonite Bottlers Limited; The Coca-Cola Company; Government of Tanzania; Food and Agriculture Organization, Tanzania; Micronutrients Initiative through International Development Research Centre; Nestlé S.A.; The Procter and Gamble Company; Mrs. Martin Solow; Tanzania Tea Blenders; Task Force SIGHT AND LIFE; The World Bank, Tanzania; UNICEF, Tanzania; United Nations Development Program, Tanzania; and the World Health Organization, Tanzania. Many other organizations responded to the letter but were unable to provide assistance. The Nutrition Foundation used these contributions to support the travel and per diem of nine meeting participants. Other meeting participants were supported through the funds of other AID implementors, United Nations agencies, nongovernmental organizations, private industry, and other private and educational institutions and foundations.

The secretariat corresponded with other organizations regarding funded participants and special meetings scheduled with the XV IVACG Meeting. These organizations included the Vitamin A Field Support Project (VITAL), the Vitamin A Technical Assistance Program (VITAP), the International Eye Foundation (IEF), Task Force SIGHT AND LIFE, UNICEF, World Health Organization (WHO), University of Iowa, and Johns Hopkins University.

Just prior to the meeting the secretariat prepared and shipped all materials for the meeting packets; finalized schedules and contracts for rooms, services, and equipment with the Arusha International Conference Centre and the three meeting hotels; and completed banking, per diem, and travel details for participants supported through Nutrition Foundation funds.

Throughout the meeting planning, the IVACG Secretariat worked closely with the leaders of the local organizing committee at the Tanzania Food and Nutrition Centre. Specifically, the local committee assisted with meeting invitations for Tanzanian nationals, arrangements for inaugural speakers, fund raising, negotiations for simultaneous interpretation during the meeting, and logistics for three study tours. Contributions received by the local committee for the meeting funded local meeting participants, communications, and special functions during the meeting.

The secretariat distributed news releases about the meeting and the meeting report to more than 200 newsletters, professional journals, and other publications worldwide during FY92 and FY93 (see Appendix 4). Announcements concerning the meeting were featured in several publications at the close of FY92; in FY93, *Mothers and Children*, *IAPB News*, *Community Eye Health*, *NCP Bulletin*, *Journal of the American Dietetic Association*, *Xerophthalmia Club Bulletin*, AID's *Front Lines*, and the newsletter of Task Force SIGHT and LIFE published information about the meeting and the meeting report.

Many meeting participants commented on the success of the meeting and the events planned around the meeting. A summary of the participants' evaluation forms was prepared and forwarded to the Office of Nutrition and the IVACG Steering Committee for consideration. The secretariat sent thank you letters to all presenters, session chairs, and contributors for the meeting and completed all outstanding reimbursements for meeting participants. Financial reports were prepared for contributing organizations.

Having rapporteurs on three continents and the increased number of meeting presentations and participants contributed to the complexity of preparing the meeting report. Following the meeting, the secretariat received the draft meeting report from the rapporteurs and coordinated all other preparation of the meeting report. In coordination with the International Life Sciences Institute's Publications Department, the report was completed. During Q4FY93, 1400

copies of *Toward Comprehensive Programs to Reduce Vitamin A Deficiency: A Report of the XV International Vitamin A Consultative Group Meeting* were printed. More than 800 copies were distributed by the end of the fiscal year, and response to the report was very positive. (The table of contents for this report is Appendix 5).

IVACG Steering Committee

The IVACG Steering Committee met on two evenings during the XV IVACG Meeting in Arusha, 9 and 10 March 1993. Prior to March, Dr. Suttilak Smitasiri and Dr. Keith P. West, Jr., were invited to serve on the IVACG Steering Committee. Both accepted the invitation and participated in the March meetings. During those meetings, the committee discussed details of the XV IVACG Meeting, activities of the IVACG regional representatives for Africa, updates on IVACG publications, ideas for the XVI IVACG Meeting, and other future plans for IVACG. Dr. Barbara Underwood resigned as chair of the steering committee effective at the close of the 10 March meeting. On 11 March, at the request of committee members, Dr. Horwitz agreed to serve as interim chair of the steering committee until a new chair is selected. The minutes of the meeting are Appendix 6.

Prior to the XV IVACG Meeting, the IVACG Steering Committee provided input to finalize the meeting program. Steering committee members took active roles during the meeting by chairing sessions, summarizing poster sessions, and giving presentations. Following the meeting, steering committee members reviewed XV IVACG Meeting evaluations and the draft XV IVACG Meeting report.

During Q3, the steering committee reviewed a document *Report of the Informal Consultation on Vitamin A Supplements Through EPI, WHO/IVACG, 30 June-1 July 1992*. Comments received from the steering committee members were forwarded to Dr. Underwood at WHO. Later the secretariat sent copies of the final report, *Using Immunization Contacts to Combat Vitamin A Deficiency*, to the steering committee. For more information about this document please see the related section on page 8 of the annual report.

During Q4, the secretariat consulted the committee about the XVI IVACG Meeting site, dates, and theme (see section on XVI IVACG Meeting in this annual report). At the close of the fiscal year, the secretariat was completing arrangements for the next IVACG Steering Committee meeting. This meeting will be held 4-5 November 1993 in Washington, D.C. To prepare for the discussion, the secretariat sent the steering committee a list of projected IVACG activities. The secretariat also sent Dr. Sommer's comments about the XVI IVACG Meeting and IVACG's strategic placement for consideration. Later, the second draft of "Strategic Placement of IVACG in the Evolving

Micronutrient Field" was provided to the committee on behalf of Dr. Simmersbach.

IVACG Regional Representatives for Africa

During the year, the representatives summarized their activities for the Office of Nutrition and the IVACG Steering Committee. Dr. Quana'a and Dr. Kavishe met with the IVACG Steering Committee in March. IVACG activities for Dr. Pawlos Quana'a were curtailed due to the political situation in Ethiopia, his country of residence. Dr. Festo Kavishe provided assistance in Zambia and Zimbabwe and was instrumental in drafting the micronutrient section of the nutrition strategy for Africa prepared by the Organization on African Unity.

In his February 1993 report, Dr. Joseph Diallo provided information on 10 countries in French-speaking Africa. This report was translated and forwarded to IVACG Steering Committee members. Another report received from Dr. Diallo in Q4FY93 covered activities related to SightFirst for the period February through July 1993. Dr. Diallo also provided a copy of this latter report to the organizers of the vitamin A meeting held in Accra in August 1993. This report may be translated for distribution to the IVACG Steering Committee at their November 1993 meeting.

Copies of new IVACG publications were provided to the representatives for distribution in their regions of Africa. The regional representatives were consulted about invitations for the XV IVACG Meeting.

Task Force Activities

Task Force on the Integration of Vitamin A Distribution with Immunization Programs

An IVACG task force began preparing "Guidelines for the Use of Vitamin A in Immunization Programs" in Q2FY89. This short document was to provide both a brief rationale and practical guidance for implementation. Unexpected criticisms of the text surfaced during FY90 related to efficacy, safety, and operational issues surrounding incorporation of vitamin A supplements into the current Expanded Programme on Immunization (EPI) schedule. Resolution of these issues occurred through correspondence and an informal consultation sponsored by WHO and IVACG in FY92. The revised document resulting from these deliberations was based on drafts developed earlier by the IVACG task force.

During FY93, the secretariat wrote to Dr. Clugston and Dr. Underwood on behalf of the IVACG Steering Committee to endorse the revised draft document. This draft was submitted as an information document to the

Expanded Programme on Immunization/Global Advisory Group (EPI/GAG) during their October 1992 meeting. The document was well-received by EPI/GAG.

Later, the WHO Nutrition Unit decided to complete the document as a report of an informal WHO consultation held 30 June-1 July 1992. The secretariat received this report; it was forwarded to Dr. Horwitz and Dr. Davidson and later circulated to the IVACG Steering Committee. Comments received were forwarded to Dr. Underwood with a letter from Dr. Horwitz and Dr. Davidson. This letter confirmed the earlier agreement to cosponsor the meeting report.

In Q4FY93, the secretariat received copies of the report of the informal WHO consultation under the title *Using Immunization Contacts to Combat Vitamin A Deficiency* (see Appendix 7). IVACG's contribution is noted on the front cover and on the inside cover page of the report. The secretariat sent this document to members of the original IVACG Task Force, IVACG Steering Committee members, and IVACG regional representatives for Africa. The WHO Nutrition Division is responsible for worldwide distribution of this document.

Assessment Methodology Task Force

A Brief Guide to Current Methods of Assessing Vitamin A Status became available for distribution during Q3FY93 (see Appendix 8). This book is an introduction to various current dietary, physiological, biochemical, histological, and clinical procedures for the assessment of vitamin A deficiency. Investigators and program planners may use the text in selecting assessment methodologies best suited to their specific situations and available resources. Each chapter includes a brief description of a procedure, a discussion of its advantages and limitations, information about interpretation of the data obtained from the method, and an example of its application. Key references for each procedure aid the reader in gathering more detailed information.

Task force members and editors, Dr. Barbara Underwood and Dr. James Olson, began preparing this monograph during FY91 and continued its refinement in FY92. During FY93, the editors and secretariat addressed final comments from reviewers. Following copy-editing, the manuscript was otherwise prepared for printing.

A news release concerning *A Brief Guide to Current Methods of Assessing Vitamin A Status* was circulated to newsletters, professional journals, and other publications worldwide. Information from this release will be included in the November 1993 issue of *Xerophthalmia Club Bulletin* and in the next issue of the newsletter of the South East Asia Nutrition Research cum Action Network. The secretariat expects additional pick up from the news release during Q1 and Q2 of FY94. A flyer publicizing this new monograph was available during the XV IVACG Meeting. Copies of the book were available for distribution at the

West African Meeting on Vitamin A Deficiency held in Accra, Ghana and at the Latin American Regional Vitamin A Meeting in Recife, Brazil.

By the close of FY93, more than 700 copies of the monograph had been distributed from the 3500 copies printed.

Other Task Forces

The secretariat included revision of the IVACG publication *Guidelines for the Development of a Simplified Dietary Assessment to Identify Groups at Risk for Inadequate Intake of Vitamin A* in the FY93 Workplan. During their March meetings, the IVACG Steering Committee discussed the potential revision and decided that Dr. Keith West would chair a new task force to review the strengths and limitations of the *Guidelines* and make recommendations for strengthening the method and other dietary assessment methods for vitamin A intake. At the close of the fiscal year, Dr. West was preparing the draft terms of reference for the task force and a list of suggested task force members. These will be discussed during the steering committee meeting in Q1FY94.

There was no action this fiscal year on other proposed task forces such as the Task Force on the Effect of Food Preparation on the Vitamin A Content of Meals and the Task Force on Community Level Programs. These and other task forces have been discussed at various times with the IVACG Steering Committee.

Other IVACG Activities

Collaboration and Liaison Activities

Fund raising, invitations, and other communications about the XV IVACG Meeting provided a new opportunity to share information about IVACG with several United Nations agencies, numerous foundations, many food and pharmaceutical corporations, and various service organizations worldwide. These communications may be valuable for future IVACG work at regional and international levels. For more specific information about these communications please see the section of this annual report "XV IVACG Meeting."

Distribution of *Toward Comprehensive Programs to Reduce Vitamin A Deficiency: A Report of the XV International Vitamin A Consultative Group Meeting* should enhance requests for collaboration regarding the XVI IVACG Meeting. The IVACG Secretariat has been in regular communication with Thai colleagues in preparation for the XVI IVACG Meeting. Liaison activities related to this meeting will increase throughout FY94.

The summary of the workshop *Coordinated Strategies for C Micronutrient Malnutrition* was published in the May 1993 *Journal of* (volume 123, pp 775-787). This workshop, sponsored by the sec parent organization - the International Life Sciences Institute, PAMM U.S. Centers for Disease Control, was held in Novembe Representatives of IVACG participated and information concerning v deficiency is included in the summary. The secretariat is distributing of the summary to all who request the article.

The news release and order forms for *Nutrition Communications in V Programs: A Resource Book* were distributed at a workshop orga PAMM in December 1992, and copies of the book were prov participants in the fall 1993 PAMM training course. Information about was available at the International Conference on Nutrition (ICN) in D 1992 courtesy of the Academy for Educational Development.

Helen Keller International distributed IVACG information and publicatic forms during a workshop on micronutrients they organized for the IC June 1993, the secretariat had the privilege of participating in a Congi briefing on the ICN organized by the Congressional Research Service. *Communications in Vitamin A Programs: A Resource Book* was availab Congressional staff attending the briefing. The secretariat's organization, ILSI, submitted comments to the U.S. Department of Ag and the U.S. Department of Health and Human Services on 7 Septemb regarding the development of the U.S. Plan of Action in respons International Conference on Nutrition. In these comments, ILSI urged c support for USAID's efforts in controlling micronutrient malnutrition a strong support for food fortification, based on sound scientific criter plan. The secretariat also participated in a public hearing on the U.S. Action.

IVACG publications were displayed at the Micronutrient Forum conjunction with the Twentieth Session of the Subcommittee on Nut the U.N. Administrative Committee on Coordination (ACC/SCN) secretariat gave a brief statement about IVACG activities including IVACG Meeting.

The secretariat also participated in a one-day forum, "Industry Partne Combatting Malnutrition" on 18 March 1993 sponsored by PAMM purpose was to explore ways to bring governmental and private secto closer together in the alliance to eliminate micronutrient malnutrition.

The secretariat arranged for the AID Office of Nutrition Director to be to the annual meeting of the International Life Sciences Institute (I which the Nutrition Foundation is a division. Mr. Seifman addressed FAO/WHO Coordinating Committee meeting and suggested wa

processing companies might aid developing countries in reaching the goals agreed to at the International Conference on Nutrition.

The secretariat participated in the Pan American Health Organization's (PAHO) Meeting of Interagency Coordination on Micronutrient Deficiency Control on 16 April 1993. The meeting focussed on the current status of micronutrient deficiencies in Latin America and the interventions being used to address them. Other participants included USAID, FAO, IEF, ICCIDD, PAMM, UNICEF, VITAL, and WHO.

IVACG regional representative for Africa Dr. Festo Kavishe represented IVACG at the West African Meeting on Vitamin A Deficiency, 9-11 August 1993 in Accra, Ghana. Several IVACG Steering Committee members also participated. According to Mr. Seifman, *A Brief Guide to Current Methods of Assessing Vitamin A Status* was very popular at this meeting.

Based on experience at the Ghana meeting, copies of *A Brief Guide to Current Methods of Assessing Vitamin A Status* were provided to VITAL for distribution during a Latin American regional meeting in Recife, Brazil, 22-26 August 1993. Selected abstracts from the XV IVACG Meeting were provided to VITAL for translation into Spanish and then distributed at the Recife meeting.

Using Immunization Contacts to Combat Vitamin A Deficiency became available from WHO during Q4FY93. IVACG's collaboration is noted on the front cover and on the inside cover page of the report. (Please note related section on page 8 of this annual report).

UN agencies continue to look to IVACG publications as significant resources to solve the problem of vitamin A deficiency. During this quarter, UNICEF, WHO, and FAO requested shipments of new IVACG publications for distribution among agency staff worldwide. ILSI's Human Nutrition Institute, of which the Nutrition Foundation is a division, has initiated jointly with FAO the development of a food-based strategies manual for controlling micronutrient malnutrition. An organizational meeting was held in Rome on 20-22 September 1993.

During Q4, Ms. Aomari met Ms. Carolyn O'Neil, Managing Editor and Correspondent for Cable News Network. Ms. O'Neil expressed interest in doing a story on vitamin A deficiency sometime in early 1994. Ms. Aomari began preliminary calls to facilitate arrangements for the story and will continue with this activity during Q1FY94.

Other collaboration and liaison during the year included the provision of IVACG documents and other resources for physicians participating in "Operation Restore Hope" for Somalia and confirmation of information for a revision of *A Field Guide for Adding Vitamin A Interventions to PVO Child Survival Projects.*

(This book was originally published in 1989 by the PVO Child Survival Sup Program of The Johns Hopkins University.) The National Academy of Scien called upon the IVACG Secretariat in Q4 to recommend reviewers for vita A-related proposals. The secretariat also provided publications and referrals the nonprofit "Watch Program" of General Injectibles and Vaccines, Inc. company is interested in developing an appropriate vitamin A supplement t could be distributed with their shipments of medical supplies and equipmen developing countries.Visitors to the IVACG Secretariat during FY93 inclu Chinese colleagues Dr. Han Ya-Shan and Dr. Wen Zhi-mei; Dr. Clive We Wageningen Agricultural University; and Mr. Steve Wilbur, Helen Ke International, Indonesia.

Joint Micronutrient Consultative Group (JMCG)

Dr. Abraham Horwitz, Dr. Barbara Underwood, and Dr. Keith West, all memb of the IVACG Steering Committee, took part in various JMCG meetings. Horwitz and Dr. West also served as members of the Joint Micronutri Mission to the Philippines in June 1993. Dr. Horwitz was the mission te chairman.

A full description of the JMCG activities can be found on pages 24 and 2

/ACG Publications

During FY93, the secretariat responded to 692 requests for IVACG docume or information related to vitamin A (see Figure 1, page 26). This year's grea number of requests, in comparison with previous years during this cooperat agreement, can be attributed to publicity for new IVACG publications, significant liaison activities of the secretariat staff, and the publicity a attendance for the XV IVACG Meeting. IVACG's new publications this y are:

- *Nutrition Communications in Vitamin A Programs: A Resource Book*
- *A Brief Guide to Current Methods of Assessing Vitamin A Status*
- *Toward Comprehensive Programs to Reduce Vitamin A Deficiency: A Rep of the XV International Vitamin A Consultative Group Meeting*

News related to IVACG publications is summarized below. Information relat to publications distribution at meetings is included in the section of this ann report titled "Collaboration and Liaison Activities."

Nutrition Communications in Vitamin A Programs: A Resource Book beca available for distribution during Q1FY93 (see Appendix 9). This publicati was the result of work begun by an IVACG task force in 1986. It summariz

basic methodological issues associated with planning, developing, and implementing nutrition communications activities. The book describes and gives examples of communications activities and their associated creative materials, provides a list of recommended readings, and outlines successful efforts undertaken in seven countries. Color photographs of printed materials and field activities plus English translations of scripts from radio and television spots are included. The book is intended for nutritionists and communications experts involved in vitamin A programs and other health and nutrition programs.

The secretariat sent copies of *Nutrition Communications in Vitamin A Programs: A Resource Book* to the many individuals and organizations that contributed to the development of this important IVACG reference. A news release concerning the book was widely circulated. Announcements concerning the book were printed in *Journal of the American Dietetic Association* (circulation 66,982); *Xerophthalmia Club Bulletin*; *Health Action Monthly*; FAO's *Food, Nutrition, and Agriculture*; the International Training in Health *List of Free Materials in Family Planning and Maternal and Child Health*; *Development Communication Report*; *Nutrition Today*; *Mothers and Children*; UNICEF's *First Call For Children*; *Vitamin A NewsNotes*; *ILSI News*; *Child Survival - World Development Newsletter*; and *Africa News*. Editors for the *Journal of Nutrition Education* (readership of approximately 30,000) and the *Indian Journal of Pediatrics* requested copies for review sections of these journals.

Information about *Nutrition Communications in Vitamin A Programs: A Resource Book* was available at a workshop organized by PAMM in December 1992 and was used as a resource during the PAMM training in the fall of 1993. Information about the book was also available at the International Conference on Nutrition (ICN) and a VITAL workshop in Uganda. During their meeting in Arusha, the IVACG Steering Committee recommended that the secretariat develop a proposal for translating this monograph into French and Spanish. The secretariat will complete this proposal during Q1FY94.

During Q3FY93, the secretariat completed *A Brief Guide to Current Methods of Assessing Vitamin A Status*. By the close of FY93, more than 700 copies of the monograph had been distributed from the 3500 copies printed. (For more detail, please see the section titled Assessment Methodology Task Force earlier in this annual report and Appendix 8.)

During Q4FY93, 1400 copies of *Toward Comprehensive Programs to Reduce Vitamin A Deficiency: A Report of the XV International Vitamin A Consultative Group Meeting* were printed. More than 800 copies of *Toward Comprehensive Programs to Reduce Vitamin A Deficiency* were distributed by the end of the fiscal year and response to the report was very positive. (For more detail about the report and related publicity, please see the earlier section concerning the XV IVACG Meeting in this annual report, Appendix 4, and Appendix 5.)

The secretariat included revision of the IVACG publication *Guidelines for the Development of a Simplified Dietary Assessment to Identify Groups at Risk for Inadequate Intake of Vitamin A* in the FY93 Workplan. Instead, a new task force will review the strengths and limitations of the *Guidelines* and make recommendations for strengthening the method and other dietary assessment methods for vitamin A intake. (For more detail, please see the earlier section "Other Task Forces" in this annual report.)

IVACG continued to support publication of *Xerophthalmia Club Bulletin* during this fiscal year. This newsletter has been cosponsored by IVACG and Sight Savers for several years. It is produced in the United Kingdom under the editorship of Dr. Donald McLaren. Issues 51, 52, and 53 were printed and distributed during this fiscal year and are Appendix 10. The IVACG Secretariat provided information for each issue, i.e., information about the XV IVACG Meeting, news releases about the XV IVACG Meeting and new publications, and abstracts from the XV IVACG Meeting. At the close of FY93, the secretariat provided an advance to the editor for issue 54.

International Nutritional Anemia Consultative Group (INACG)

Introduction

The Nutrition Foundation, Inc. first received financial support as the secretariat for INACG in 1977. Funding continued through a series of grants and extensions until the present cooperative agreement began 1 October 1987. This cooperative agreement was for five years, but was extended to cover FY93. Thus this annual report covers the sixth year of the cooperative agreement.

The mission of INACG is to facilitate the efforts of United Nations agencies, bilateral agencies, governments, private voluntary and non-governmental organizations, and private industry to reduce nutritional anemia and its consequences by providing guidance and know-how through an established international network of experts. In carrying out this mission, INACG sponsors international meetings and scientific reviews and convenes task forces to analyze and make recommendations related to the etiology, treatment, and prevention of nutritional anemias. Task force reports provide guidelines and strategies to assess the prevalence of nutritional anemias; refine assessment techniques; and develop, monitor, and evaluate intervention programs. The examination of these issues is important to the establishment of public policy and action programs.

INACG guidelines and strategies are generally disseminated through INACG's state-of-the-art monograph series. These monographs, along with INACG meeting reports, achieve worldwide circulation through channels of the United Nations agencies, AID, and other international aid agencies, nongovernmental organizations, educational institutions, and private industry, and through direct correspondence with professionals working in developing countries.

The INACG Secretariat provides managerial, administrative, and logistic support for the INACG Steering Committee and all INACG activities. The steering committee consists of at least five members, including one representative from each of AID's three geographic regions (Latin America-Caribbean, Asia-Near East, and Africa), as well as the AID project officer for INACG. A list of the current steering committee members is included as Appendix 11.

In carrying out its responsibilities, the secretariat collaborates closely with the AID Office of Nutrition. Dr. Samuel G. Kahn, Senior Nutrition Advisor at the Office of Nutrition, serves as secretary of INACG and the AID project officer for INACG.

XII INACG Meeting: Combating Iron Deficiency Anemia Through Food Fortification Technology

French and Spanish translations of the action plan developed at this meeting, held in December 1990, were printed and distributed to individuals on the INACG list from French- and Spanish-speaking countries (see Appendix 12).

INACG Steering Committee

The steering committee met in Arusha, Tanzania, on 12 March 1993. This site and date were selected to coincide with the XV IVACG Meeting. One session during the XV IVACG Meeting was devoted to other micronutrients of public health importance. Dr. James Cook gave a presentation on the current status of iron deficiency anemia, assessment methodologies, and effective interventions.

The minutes of the steering committee meeting are in Appendix 13. Dr. Cook took part in the steering committee meeting as did Dr. Festo Kavishe, Director of the Tanzanian Food and Nutrition Centre. Dr. Kavishe provided valuable insights into iron deficiency anemia interventions in his country. The committee heard an update on the activities of the Group for the Control of Iron Deficiency Anemia (GCID) from Dr. Fernando Viteri as well as an update on the progress of the various task forces from the secretariat. The components of a plan of action to guide the work of INACG over the next year were adopted. The secretariat drafted the plan of action after the meeting and circulated it for comment. The final version based on the comments received was circulated to the full steering committee (Appendix 13).

For the first time an INACG Directory (Appendix 14) was made available to the steering committee members. This directory lists the individuals who responded to an information letter describing INACG and its activities. The secretariat maintains the list and sends information on INACG publications and activities to these people.

There were two changes in the make-up of the steering committee this year. Dr. Maletnlema resigned because of his retirement. Dr. Louis Sullivan, President of Morehouse Medical School and the former Secretary of the U.S. Department of Health and Human Services, joined the steering committee. Dr. Sullivan is a hematologist by training, and he made important contributions to the understanding of nutritional anemias early in his career.

Task Force Activities

Task Force on NaFeEDTA

This task force comprised of Dr. Sean Lynch, Chairman, Dr. Thomas Bothwell, Dr. Patrick MacPhail, and Dr. Richard Hurrell, completed their work during the year, and a monograph entitled, *Iron EDTA for Food Fortification*, was published and distributed (Appendix 15). Dr. George Bates, Dr. John Vanderveen, and Dr. Paul Whittaker joined Dr. Samuel Kahn and the secretariat in reviewing the draft monograph. Their comments were addressed in completing the final draft. Eight hundred copies were printed.

In addition to preparing the monograph for publication, the secretariat commissioned Dr. Ian Munro, CanTox, Inc., to prepare a toxicology monograph and specifications data sheet for submission to the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Dr. Munro drew heavily on the information compiled by the task force in writing these documents. The monograph and specifications data sheet are in Appendix 16.

JECFA met in February 1993 and reviewed the material supplied by Dr. Munro and granted a provisional approval for sodium iron EDTA for use in supervised food fortification programs in developing countries where iron deficiency anemia is a public health problem (Appendix 17). This is the first time an international body or a national regulatory agency approved the use of iron EDTA based on safety data. JECFA asked that some additional information be gathered and submitted. These are actual food-grade purity specifications from a supplier and additional studies to assess the site of deposition of iron administered as sodium iron EDTA and to assess the metabolic fate of the whole molecule following long-term administration.

The secretariat sent letters to all suppliers of EDTA salts and to food companies that produce iron-fortified products informing them of JECFA's action and encouraging them to provide specifications data should they begin to produce or use food-grade sodium iron EDTA. The secretariat along with Dr. Sean Lynch and Dr. Sam Kahn, worked with a consultant for the World Bank who is developing supplemental foods fortified with iron for pregnant and lactating women and young children in Ecuador. After reviewing the INACG monograph and the JECFA submission, the consultant, Dick Uiterwaal, recommended the use of sodium iron EDTA at appropriate concentrations to the Ecuadorian Ministry of Health. This recommendation was approved pending the outcome of preliminary acceptance tests.

Task Force on the Relationship of Anemia to Mental and Behavioral Development

No action was taken by this group during FY93. A draft publication modeled after the *Guidelines for the Control of Maternal Nutritional Anemia* was prepared in FY92 and was reviewed by the steering committee. The AID project officer, Dr. Samuel Kahn, asked the secretariat to develop a new design for the publication taking the comments of the steering committee on content into consideration. The secretariat will undertake this task in FY94.

Blood Spot as an Iron Status Assessment Tool

During Q4FY93, the secretariat, at the direction of the AID project officer and Mr. Richard Seifman, Director, Office of Nutrition, contacted Dr. James Cook to explore the possibility of a one-day workshop on the efficacy of the blood spot as an iron deficiency assessment tool. Dr. Cook felt strongly that this tool was effective for measuring hemoglobin, but data judging its efficacy for more specific measures of iron status, e.g., serum ferritin and transferrin, were not yet available. For this reason no meeting was arranged.

The secretariat did an on-line literature search for articles describing the blood spot hemoglobin test and provided this list to the AID project director.

Other INACG Activities

Research Project to Determine the Effectiveness of Iron-fortified Infant Cereal in the Prevention of Iron Deficiency Anemia

Dr. Tomas Walter, Head of the Hematology Unit, Instituto de Nutricion y Tecnologia de los Alimentos (INTA) in Chile and a member of the INACG Steering Committee, published the results of this research in *Pediatrics* in May 1993 (see Appendix 18). INACG played a pivotal role in planning this research project, which was administered through the Nutrition Foundation with funds from the Gerber Products Company. The major finding was iron-fortified infant rice cereal can contribute substantially to preventing iron deficiency anemia.

Collaboration with Other Groups Active in Nutritional Anemia Programs

The Nutrition Foundation, Inc. exhibited INACG publications at the Micronutrient Fair held during the Program Against Micronutrient Malnutrition's (PAMM) Advocacy Week in Atlanta, Georgia, on 3 December 1993. In addition, ILSI's Human Nutrition Institute worked with PAMM to organize a forum on the role of the food industry in controlling micronutrient malnutrition. Three speakers were involved: Dr. Jon Rohde, UNICEF; Mr. Richard Hanneman, The Salt Institute; and Dr. David Yeung, H.J. Heinz Company. There was

considerable discussion about the positive role of food fortification in controlling iron deficiency anemia.

During the International Conference on Nutrition, the Nutrition Foundation aided the Helen Keller International (HKI) and the International Council for Control of Iodine Deficiency Disorders (ICCIDD) by arranging for Dr. George Purvis to present a short talk on iron fortification at their micronutrient workshop. There was enthusiastic discussion of the benefits of food fortification following his presentation.

INACG publications were displayed at the Micronutrient Forum held in conjunction with the Twentieth Session of the Subcommittee on Nutrition of the U.N. Administrative Committee on Coordination (ACC/SCN). The secretariat also provided a brief statement about INACG activities.

The secretariat also participated in a meeting of the National Academy of Sciences Food and Nutrition Board's Committee on Prevention and Control of Iron Deficiency Anemia among U.S. Children and Women of Childbearing Age. The secretariat encouraged the committee to consider the impact of guidelines they will develop on developing countries. While these countries are not the target audience for the committee, they read what the committee publishes. Copies of the INACG Action Plan were distributed, and the group was informed of the JECFA decision on sodium iron EDTA.

A report of INACG's 1992 activities was prepared by the secretariat for the International Union of Nutritional Sciences (IUNS). This report will be a part of the IUNS annual report.

The summary of the workshop *Coordinated Strategies for Controlling Micronutrient Malnutrition* was published in the May 1993 *Journal of Nutrition* (volume 123, pp 775-787). This workshop, sponsored by the secretariat's parent organization, the International Life Sciences Institute, PAMM, and the U.S. Centers for Disease Control, was held in November 1991. Representatives of INACG participated in the workshop.

The secretariat participated in the Pan American Health Organization's (PAHO) Meeting of Interagency Coordination on Micronutrient Deficiency Control on 16 April 1993. The meeting focussed on the current status of micronutrient deficiencies in Latin America and the interventions used to address them. Other participants included AID, FAO, International Eye Foundation, ICCIDD, PAMM, UNICEF, VITAL, and WHO.

Through the ILSI Human Nutrition Institute, the secretariat has participated in several activities related to the U.S. Plan of Action being written in response to the International Conference on Nutrition. These include a Congressional briefing organized by the Congressional Research Service; participation in a

public hearing on the U.S. Plan of Action; and submission of written comments on what the Plan should address.

Joint Micronutrient Consultative Group (JMCG)

Dr. James Cook continued to serve as INACG's representative in the Joint Micronutrient Consultative Group, along with Dr. Richard Theuer, Chairman of the INACG Steering Committee. Dr. Cook also participated in the Joint Micronutrient Mission to the Philippines in June 1993. See pages 24-25 for a complete description of JMCG activities.

INACG Publications

During fiscal year 1993, the secretariat published or prepared the following documents:

- *Combating Iron Deficiency Anemia Through Food Fortification Technology: An Action Plan* in French and Spanish
- *Iron EDTA for Food Fortification*
- A toxicology monograph on sodium iron EDTA prepared for JECFA *(WHO Food Additives Series 32, Toxicological evaluation of certain food additives and contaminants*, World Health Organization, Geneva, 1993, Pages 195-222.

The total number of requests for INACG information and publications received was 385 (Figure 2). This is an increase over the total of 325 requests in FY92.

International Nutrition Planners Forum (INPF)

Introduction

The International Nutrition Planners Forum (INPF) is an informal organiz professionals from developing countries with expertise and responsibi food and nutrition-related policies and programs. INPF provides opport and channels of communication for participants to exchange ide experiences; learn from one another; discuss common nutrition proble possible solutions; formulate policy and technical recommendations; points of view of developing countries known internationally; and inf important decisions made by international organizations and donors.

The Nutrition Foundation, Inc. has served as the INPF secretariat since providing managerial, administrative, and logistic support to INPF and th Steering Committee. This function was extended through FY93 by AI INPF Steering Committee consists of seven members, includin representatives from each of AID's three geographic regions (Latin Ar Caribbean, Asia-Near East, and Africa), and the AID project officer fo A list of INPF Steering Committee members is included as Appendix 19 report.

INPF Steering Committee

A steering committee meeting was held 7 March 1993 in Arusha, Tar during the XV IVACG Meeting. Minutes of the meeting are in Appendi this report. The committee heard three presentations about nutrition n development at a regional level. One was given by Ms. Catherine Sian Coordinator of the Food and Nutrition Program for the Commonwealth Re Health Community Secretariat for East, Central, and Southern (CRHCS/ECSA). The others were provided by Dr. Wynante Patter member of the steering committee, regarding the work of the Caribbea and Nutrition Institute in Jamaica, and Dr. Jamie Ariza, also a s committee member and President of the Latin American Society of Nu As a result of these discussions, Ms. Siandwazi and Mrs. Julia Tagwireyi Dr. Patterson in Jamaica to gain additional insights into ways to stre nutrition networks.

The steering committee restated the goals, objectives, and activities o (see Appendix 21). In keeping with these ideas, the steering com organized an ad hoc workshop on 30 September 1993 during th International Congress of Nutrition in Adelaide, Australia. The purpose workshop was to share experiences in developing effective nu communication programs. The draft agenda for the workshop is in Ap 22.

INPF Publications

During FY93, the French and Spanish translations of the report of the Sixth INPF Conference, *Effective Nutrition Communication for Behavior Change*, were completed, and 800 copies of each printed. These were distributed to appropriate AID missions and to the French- and Spanish-speaking participants at the workshop. A news release announcing the availability of these translations was distributed to the Nutrition Foundation news release mailing list (see Appendix 23).

The secretariat received 272 requests for INPF information and publications (Figure 3), an increase from the FY92 total of 75.

Joint Micronutrient Consultative Group (JMCG)

Introduction

The Nutrition Foundation, Inc. established the Joint Micronutrient Consultative Group (JMCG) in fiscal year 1992 in response to a modification in the cooperative agreement with the Office of Nutrition. The purpose of the group is to explore using an integrated approach to micronutrient malnutrition interventions. JMCG represents an evolving process whereby the intellectual resources of INACG, IVACG, and ICCIDD are brought together.

During the first year, the group focussed their attention on developing a joint protocol for assessment and interventions which can be applied to iron, vitamin A, and iodine deficiencies. During fiscal year 1993, the group organized a mission to the Philippines to test the concept of an integrated approach in-country.

JMCG Meetings

The JMCG met in Washington on 23 October 1992 to discuss the next phase in developing an integrated approach to control micronutrient deficiencies. Representatives of INACG, IVACG, and ICCIDD were present along with representatives of the AID Office of Nutrition and the World Bank. Minutes of the meeting and a list of attendees are in Appendix 24. Having completed development of a "Coordinated Assessment Methodology" matrix, the group discussed possible joint intervention strategies.

Mr. Richard Seifman, AID Office of Nutrition, challenged the group to consider testing the integrated approach by sending a team of micronutrient experts to work in a developing country with local leaders to develop a country-specific plan for integrated assessment, intervention, and evaluation strategies. The group discussed criteria for country selection and outlined terms of reference for such a project. Countries were considered for the mission with the Philippines emerging as the first choice.

Joint Micronutrient Mission

During the International Conference on Nutrition in Rome in December 1992, Mr. Seifman met with Dr. Jaime Z. Galvez Tan, Chief of Staff and Undersecretary of Health in the Philippines, to discuss the possibility of organizing a joint mission on micronutrient malnutrition. Dr. Tan enthusiastically agreed to participate in this mission.

A micronutrient mission team, consisting of Dr. Abraham Horwitz as chairman, Dr. James Cook, Dr. John Dunn, and Dr. Keith West, met on 14-15 January

1993 to finalize the terms of reference for the mission and the scope of work. These were forwarded to Dr. Tan for input from the Philippine National Nutrition Council.

Several members of the team met with representatives from the Philippines during the XV IVACG Meeting in Arusha, Tanzania, in March 1993. These discussions provided additional insight into the micronutrient deficiency programs currently operating and plans for future programs. Mr. Rolf Klemm, Helen Keller International, Philippines, offered to help the mission team in communicating with Filipino officials and in making logistical arrangements.

On 21 April 1993, members of the Joint Micronutrient Mission Team met with Dr. Tan in Washington, D.C. to finalize plans for the team's visit to the Philippines on 12-26 June 1993. The secretariat prepared briefing books for team members, which included information about ongoing and planned micronutrient activities in the Philippines. The secretariat also made all necessary logistical arrangements for the team's visit and established contact with the AID mission in Manila. The terms of reference for the mission and the scope of work are in Appendix 25 of this report.

Two conference calls for team members were organized in May to finalize the mission agenda and to outline the mission report. The report will include an evaluation of the process and its applicability to other countries. Ms. Lynnda Keiss, AID Office of Nutrition, was assigned to accompany the team to the Philippines and help prepare the report.

Following the successful completion of the mission, the secretariat drafted thank you letters for Dr. Horwitz to send to the leaders of the Philippine team. The secretariat also thanked Mr. Klemm and HKI for their support of the mission. Finally, the secretariat reviewed a draft executive summary of the mission report and provided comments to Ms. Keiss, who is responsible for compiling the report.

Follow-up

Once the mission report is finalized the secretariat plans to circulate it to the Philippine government officials involved in the mission as well as to other groups involved in micronutrient malnutrition interventions. The findings of this mission will provide valuable information about the feasibility of the mission's approach to integrating micronutrient activities.

General Cooperative Agreement Activities

Monitoring and Tracking Requests for Information

Responding to information requests is one of the secretariat's most important functions. During fiscal year 1992, the secretariat tracked such requests through an interactive database, thus facilitating the secretariat's responses to requets and the secretariat's ability to summarize information about these requests.

Figures 1, 2, and 3 give the number of requests received by quarter for IVACG, INACG, and INFP, respectively. For all three programs the number of requests exceeded the totals for FY92.

Figure 1

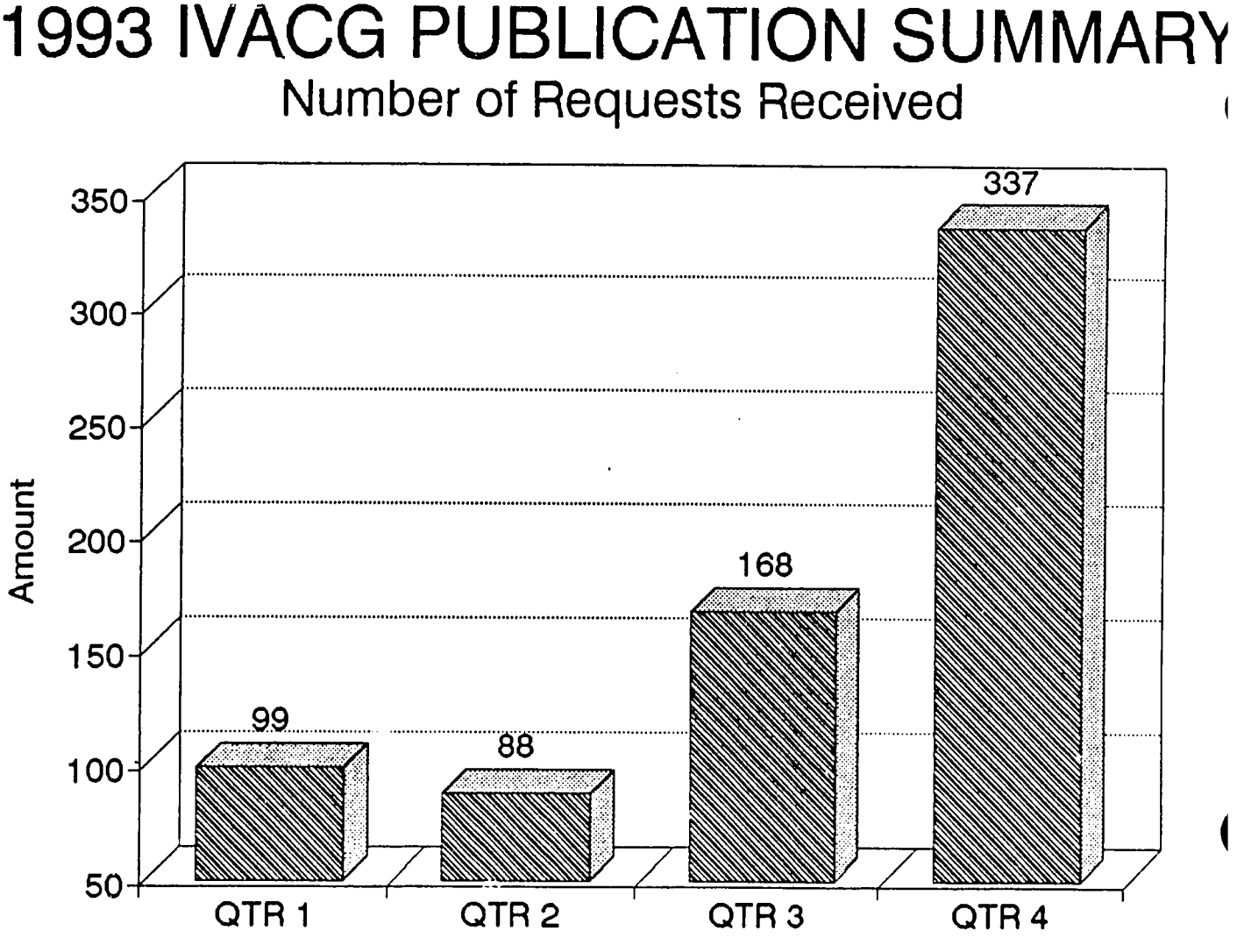


Figure 2

1993 INACG PUBLICATION SUMMARY

Number of Requests Received

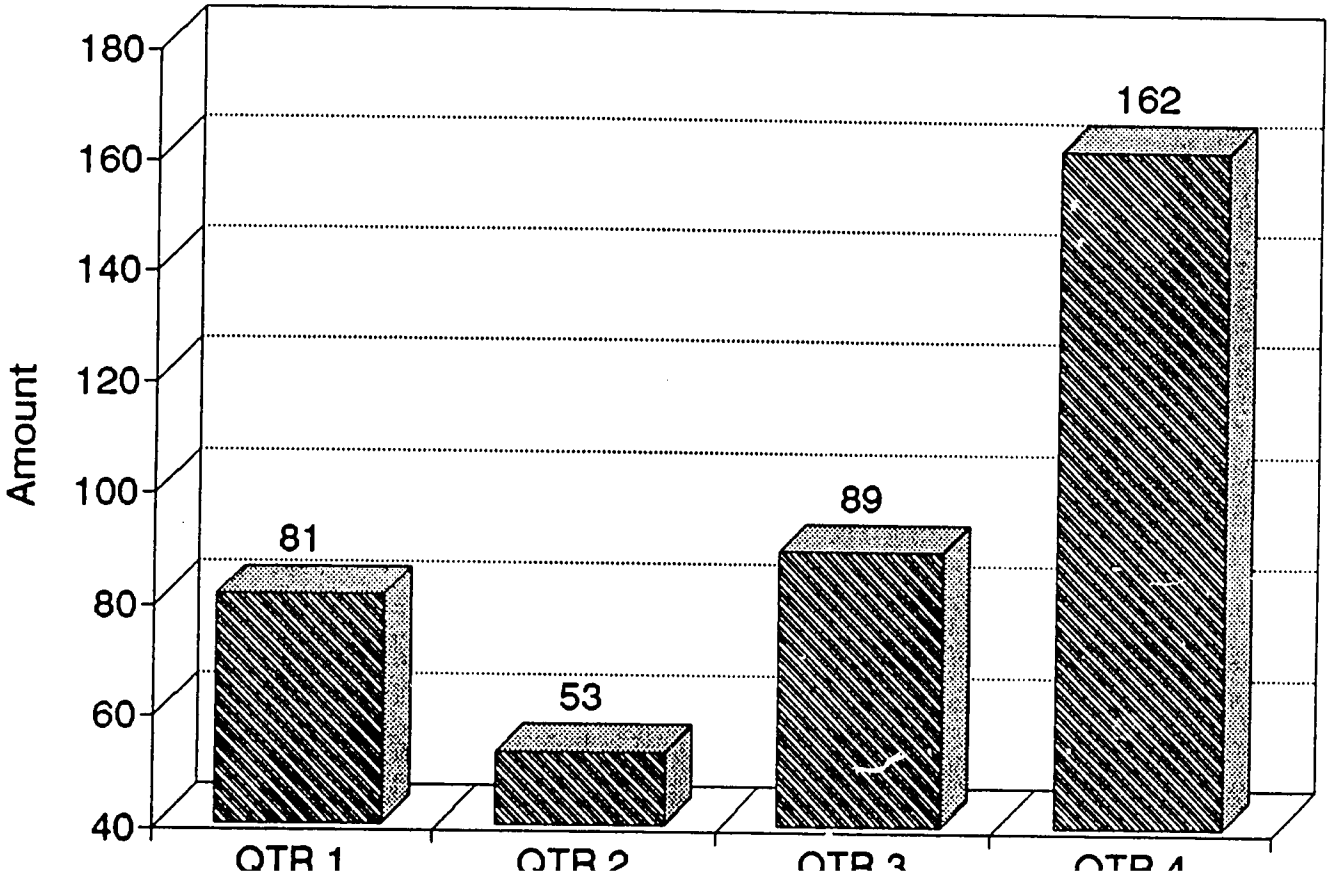
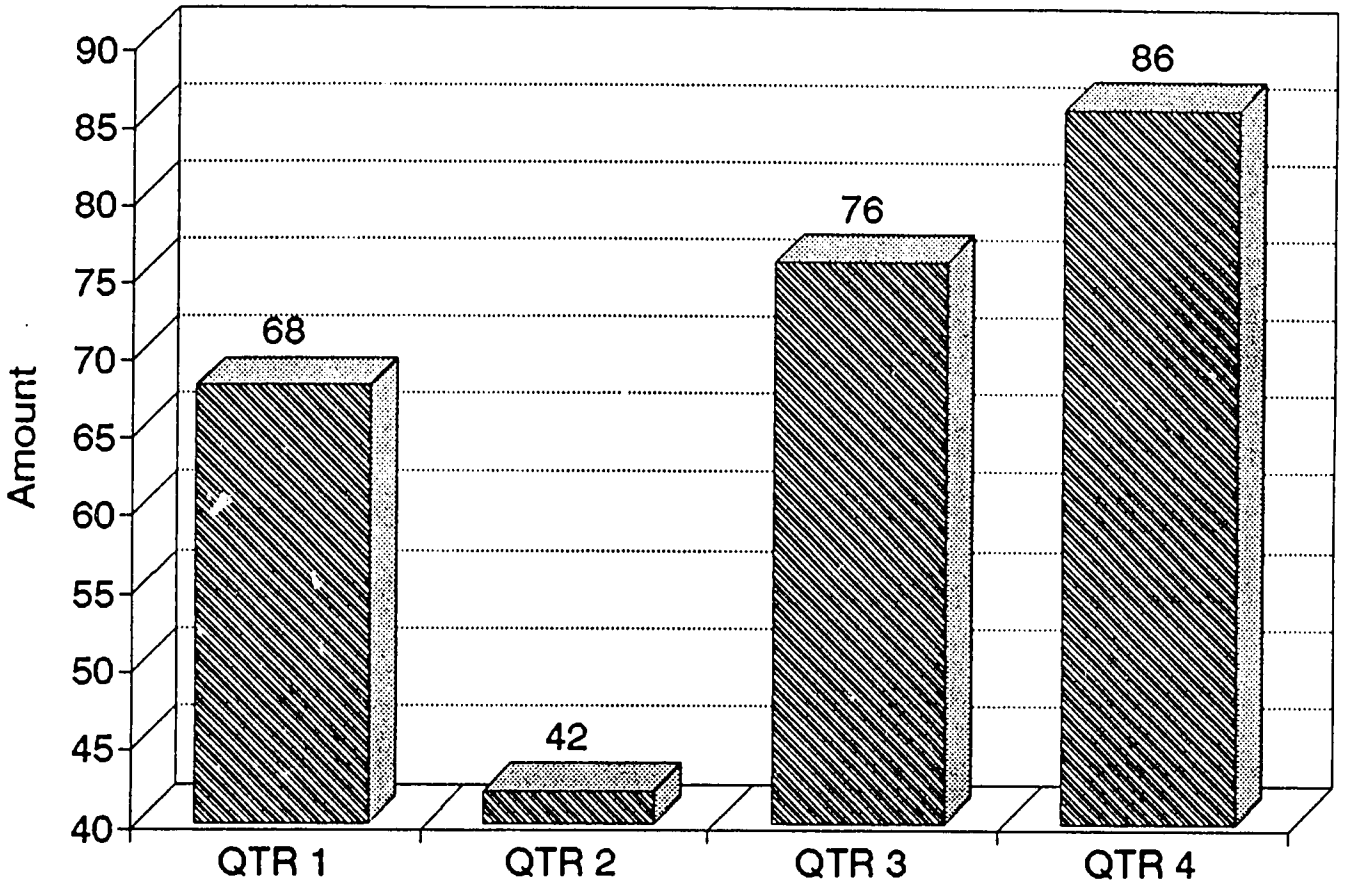


Figure 3

1993 INPF PUBLICATION SUMMARY

Number of Requests Received



Reporting Requirements

Documents required by Cooperative Agreement No. DAN-5115-A-00-7114-00 were submitted to the AID project officer, Ms. Brenda J. Colwell, and other project officers as outlined below:

	Type of Document	Date Submitted
1.	Q4FY92 report and Financial Statement	30 October 1992
2.	FY92 Annual Report	30 October 1992
3.	Draft minutes of 23 October 1992 JMCG meeting (submitted to the INACG project officer and Director of the Office of Nutrition)	6 November 1992
4.	Q1FY93 report and Financial Statement	29 January 1993
5.	Draft minutes of the 14-15 January meeting of the Joint Micronutrient Mission working group (submitted to the INACG project officer) Revised minutes (submitted to members of the Joint Mission Team, the director of the Office of Nutrition, USAID, and the IVACG/INACG project officers)	22 February 1993 9 March 1993
6.	Draft minutes of the INPF Steering Committee meeting held 7 March 1993	23 March 1993
7.	Overview of IVACG activities for Q3-Q4FY93 (submitted to the Office of Nutrition)	26 March 1993
8.	Draft minutes of the IVACG Steering Committee meetings held 9 and 10 March 1993 in Arusha, Tanzania	30 March 1993
9.	Draft minutes of the INACG Steering Committee meeting held 12 March 1993	30 March 1993
10.	Trip report related to the XV IVACG Meeting, held 8-12 March 1993 in Arusha, Tanzania	2 April 1993
11.	Summary of evaluations from the XV IVACG Meeting (submitted to the Office of Nutrition)	8 April 1993
12.	Q2FY93 report and Financial Statement	30 April 1993

13.	Draft meeting summary for the XV IVACG Meeting (submitted to the Office of Nutrition) A partial draft had been submitted earlier on 13 April 1993.	17 May 1993
14.	Draft minutes of the Joint Micronutrient Consultative Group Mission Planning Meeting held 21 April 1993 (submitted to the Office of Nutrition.	4 May 1993
15.	Q3FY93 report and Financial Statement	29 July 1993

Financial Report

Summary of Direct Expenses for Fiscal Year 1993
Cooperative Agreement No. DAN-5115-A-00-7114-00

FINANCIAL SUMMARY FOR FISCAL YEAR 1993
OCTOBER 1, 1992 THROUGH SEPTEMBER 30, 1993

	VITAMIN A	ANEMIA	SUSTAIN	INPF	INNE	TOTAL
DIRECT LABOR	75,086.01	24,858.84	0.00	2,005.62	0.00	101,950.47
FRINGE BENEFITS	22,326.33	6,565.58	0.00	543.63	0.00	29,437.54
TEMPORARY HELP	829.12	77.75	0.00	0.00	0.00	906.87
CONSULTANTS	3,900.00	2,400.00	0.00	0.00	0.00	6,300.00
PUBLICATIONS & SUPPORT	94,107.60	14,878.20	0.00	5,160.61	0.00	114,146.41
TRAVEL	64,384.10	22,748.31	0.00	18,007.32	0.00	105,139.73
PER DIEM	17,552.75	5,320.58	0.00	1,666.04	0.00	24,539.37
SUPPLIES	4,100.58	822.64	0.00	627.72	0.00	5,550.94
EQUIPMENT PURCHASE	1,787.90	0.00	0.00	0.00	0.00	1,787.90
OFFICE LEASE	13,010.70	3,595.70	0.00	507.25	0.00	17,113.65
GENERAL EXPENSES	1,519.73	1,343.77	0.00	4,477.15	0.00	7,340.65
FISCAL ADMINISTRATION	9,152.31	2,998.04	0.00	1,189.67	0.00	13,340.02
COMMUNICATIONS	33,967.98	8,586.11	0.00	2,886.00	0.00	45,442.09
MEETING ROOM RENTAL	3,555.00	0.00	0.00	0.00	0.00	3,555.00
TOTAL DIRECT	345,282.11	94,197.52	0.00	37,071.01	0.00	476,550.64
INDIRECT (12%)	41,433.85	11,303.71	0.00	4,448.53	0.00	57,186.09
TOTAL AMOUNT	386,715.96	105,501.23	0.00	41,519.54	0.00	533,736.73

Cooperative Agreement DAN-5115-A-00-7114-00

Cooperative Agreement and Overall Modification History

	Increase	Total
Initial Obligated Amount 11/23/87		$1,181,938.00
Modification #1 11/09/88	$229,000.00	$1,410,938.00
Modification #2 09/19/89	$60,000.00	$1,470,938.00
Modification #3 02/27/90	$60,000.00	$1,530,938.00
Modification #4 08/21/90	$565,000.00	$2,095,938.00
Modification #5 05/08/91	$300,000.00	$2,395,938.00
Modification #6 07/11/91	$303,000.00	$2,698,938.00
Modification #7 09/30/92	$585,882.00	$3,284,820.00
Modification #8 08/06/93	$191,444.00	$3,476,264.00
TOTAL OBLIGATED AMOUNT THROUGH 11/30/93		**$3,476,264.00**

Specific Project Allocation of Funds

	IVACG	INACG	INPF	INNE	SUSTAIN	TOTAL
Initial 11/23/87	772,991	50,000	------	------	358,947	1,181,938
Mod. #1 11/09/87	------	229,000	------	------	------	229,000
Mod. #2 09/19/89	------	------	------	------	60,000	60,000
Mod. #3 02/27/90	------	------	------	------	60,000	60,000
Mod. #4 08/21/90	300,000	150,000	85,535	15,000	14,465	565,000
Mod. #5 05/08/91	300,000	------	------	------	------	300,000
Mod. #6 07/11/91	50,000	------	228,000	25,000	------	303,000
Mod. #7 09/30/92	313,357	131,294	103,942	37,289	------	585,882
Mod. #8 08/06/93	113,007	78,437*	------	------	------	191,444
SUB-TOTALS	**1,849,355**	**638,731***	**417,477**	**77,289**	**493,412**	**3,476,264**

* An amount of $78,437 was included in amendment #8; written documentation regarding actual program distribution was not received as of 10/31/93.

List of Appendices

1. IVACG Steering Committee members
2. XV IVACG Meeting, program
3. XV IVACG Meeting, invitation
4. XV IVACG Meeting, FY 93 news release
5. *Toward Comprehensive Programs To Reduce Vitamin A Deficiency: A Report of the XV International Vitamin A Consultative Group Meeting*, table of contents
6. Minutes of the IVACG Steering Committee meetings
7. *Using Immunization Contacts to Combat Vitamin A Deficiency*
8. *A Brief Guide to Current Methods of Assessing Vitamin A Deficiency*, table of contents and news release
9. *Nutrition Communications in Vitamin A Programs: A Resource Book*, table of contents and news release
10. *Xerophthalmia Club Bulletin*, issues 51, 52, and 53
11. INACG Steering Committee members
12. INACG Action Plan, news release for translations
13. Minutes of the INACG Steering Committee meeting and INACG Steering Committee plan of action
14. INACG directory
15. *Iron EDTA for Food Fortification*, table of contents and news release
16. Sodium iron EDTA toxicology monograph for JECFA
17. JECFA provisional approval of sodium iron EDTA
18. *Effectiveness of Iron: Fortified Infant Cereals in Prevention of Iron Deficiency Anemia*
19. INPF Steering Committee members

20. Minutes of the INPF Steering Committee meeting

21. INPF Steering Committee goals, objectives, and activities

22. INPF draft agenda for workshop at XV International Congress of Nutrition

23. News release for translations of *Effective Nutrition Communications for Behavior Change*

24. JMCG minutes and participants

25. Terms of reference and scope of work for Joint Micronutrient Mission

Appendix 1

International
Vitamin A
Consultative
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Secretary
Dr. Frances R. Davidson, USAID

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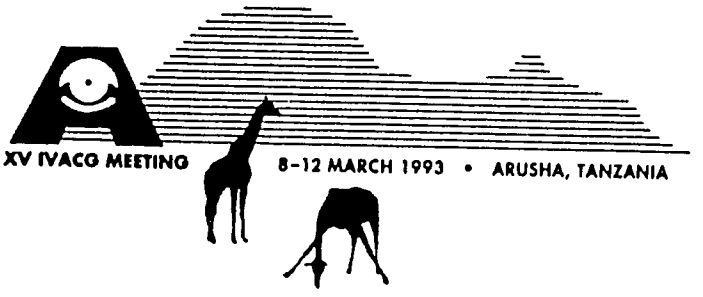
Appendix 2



Program

Views expressed by the presenters do not necessarily reflect the views of IVACG or The Nutrition Foundation, Inc.

Sunday, 7 March 1993

1800-2130	**Early Registration** at Novotel Mt. Meru Hotel

Monday, 8 March 1993

0800	**Registration continues** at Arusha International Conference Centre
	Set up for poster session: Activities for the Control of Vitamin A Deficiency in Tanzania
0900-1730	Activities for the Control of Vitamin A Deficiency in Tanzania posters on display, presenters available 1515-1600
0900	**Inauguration**
	Master of Ceremonies: Dr. Festo Kavishe, Managing Director, Tanzania Food and Nutrition Centre
	Mr. E.G. Moyo, Chair, National Vitamin A Consultative Group
	Dr. E.A. Duale, WHO Representative, Tanzania
	Mr. Dan Toole, UNICEF Delegate, Tanzania
	Dr. Frances R. Davidson, Deputy Director, Office of Nutrition, Bureau for Research and Development, US Agency for International Development
	Dr. Franz Simmersbach, Headquarters Representative, FAO
	Dr. E.A. Duale, on behalf of Dr. Gottlieb L. Monekosso, Regional Director, African Regional Office, World Health Organization
	Mr. Cole Dodge, UNICEF Representative, Regional Office
	Dr. Abraham Horwitz, Chair, International Vitamin A Consultative Group
	Mrs. Zakia Meghji, Deputy Minister of Health, Tanzania
1030	Break

Monday 8 March 1993 (continued)

1050	**National Symposium Session** Chair: Dr. B.B.O. Mmbaga
1050	An Overview of the National Programme for Prevention and Control of Vitamin A Deficiency and Xerophthalmia in Tanzania Mr. C.R. Temalilwa
1115	Vitamin A Capsule Distribution Through the Primary Health Care System: The Tanzania Experience Mr. M. Kweba
1140	Monitoring Impact Through the Sentinel Xerophthalmia Surveillance System Dr. Godwin Ndossi
1205	Discussion and announcements
1230	Lunch
1400	**National Symposium Session** Chair: Dr. Godwin Ndossi
1400	Dietary Approaches for the Control of Vitamin A Deficiency in Tanzania Mr. L. Mselle
1425	Information, Education, Communication and Training in the Vitamin A Deficiency Programme in Tanzania Mrs. Hidaya Missano
1450	Initiation of Control of Vitamin A Deficiency Through Primary Health Care Dr. B.B.O. Mmbaga
1515	Break and **Poster Session on Activities for the Control of Vitamin A Deficiency in Tanzania** with presenters available
1600	**National Symposium Session** Chair: Ms. Joyce Hamisi
1600	Public Health Measures in the Control of Vitamin A Deficiency: A Proposal to Control Intestinal Parasites Prof. C. Kihamia
1625	A Proposed Plan for Tea Fortification with Vitamin A Mr. C.R. Temalilwa
1650	Discussion and announcements
1730	End of day's formal sessions
1900	**Reception** at Novotel Mt. Meru Hotel Deputy Minister of Health and the Local Organizing Committee

Tuesday, 9 March 1993

0800	Set up for poster sessions: Program Issues and New Human Research on the Functions of Vitamin A
0900-1800	Program Issues and New Human Research on the Functions of Vitamin A poster sessions on display, presenters available 1515-1600
0900	**Projects to Programs: What does it take?** Chair: Dr. Abraham Horwitz
0910	International Perspective Mr. James Greene
0940	National Perspective Dr. Festo Kavishe
1000	National Perspectives Panel
1000	India: Dr. Vinodini Reddy
1010	Brazil: Dr. Leonor Santos
1020	Philippines: Dr. Florentino Solon
1030	Break
1100	**Programs: How do we know they are working?** Chair: Dr. Aree Valyasevi
1100	International Perspective Dr. John B. Mason
1130	National Perspective Dr. Ignatius Tarwotjo
1200	Discussion and announcements
1230	Lunch
1400	**Operational Issues Defined by Field Experience** Chair: Dr. Franz Simmersbach
1400	Cost, Coverage and Change of Health Status Associated with Alternative Approaches to the Control of Vitamin A Deficiency in Nepal Dr. Robert L. Tilden
1420	Success of Communication Programme in Reducing Vitamin A Deficiency Through Changing Dietary Habit: Worldview—Nutritional Blindness Prevention Programme Dr. Nazrul Islam
1440	Social Marketing in the Prevention and Control of Vitamin A Deficiency: An Unfinished Agenda Dr. Joseph Sclafani
1500	Discussion

Tuesday, 9 March 1993 (continued)

1515	Break and **Vitamin A Program Issues Poster Session** with presenters available
1600	**Vitamin A Program Issues** Chair: Dr. Moses Chirambo
1600	Evaluation of A Policy of Routine High Dose Vitamin A Therapy for Children Hospitalized with Measles Dr. Greg Hussey
1615	Vitamin A Supplementation in Bolgatanga-Frafra District Ghana: Costs and the Window of Opportunity for Integration with EPI Dr. Dyna C. Arhin
1630	Vitamin A Supplementation in Chikwawa District, Malawi: Mother's Knowledge, Delivery Strategies, Missed Opportunities Mr. John M. Barrows
1645	Vitamin A Status and Lactation in Indonesian Women: A Randomized Trial of High-Dose Supplementation in the Post-Partum Period Dr. Rebecca J. Stoltzfus
1700	Factors Affecting the Utilization of Community Based Micronutrient Interventions in Eastern Indonesia Dr. Peter Fajans
1715	Factors Associated with Coverage of Vitamin A Capsule Distribution in a District in Central Java, Indonesia, 1991 Dr. Hamam Hadi
1730	**Summary of Vitamin A Program Issues Poster Session** Dr. Benny Kodyat
1745	Discussion and announcements
1815	End of day's formal sessions
1915	IVACG Steering Committee dinner and meeting
1915	Demonstration of PROFILES: Computer graphics for promoting the importance of nutrition in national development (At Novotel Mt. Meru Hotel) Dr. Bart Burkhalter

Wednesday, 10 March 1993

0800-0830	Set up for poster sessions: Consequences for Human Health and Development of Vitamin A Deficiency Newer Methodologies for Assessing Subclinical Vitamin A Deficiency
0830-1800	Wednesday poster sessions on display, presenters available 1400-1445
0830	**Vitamin A and Childhood Mortality: Reports from Clinical Trials** Chair: Dr. George Beaton
0830	The Effects of Vitamin A Supplementation on Childhood Mortality in Northern Ghana Dr. David Ross and Ms. Nicola Dollimore
0900	Discussion
0915	Impact of Periodic Vitamin A Supplementation on Early Infant Mortality in Nepal Dr. Keith P. West, Jr.
0930	Discussion
0945	Effectiveness of Vitamin A Supplementation in Control of Young Child Morbidity and Mortality in Developing Countries Prof. George Beaton
1025	Break
1050	**Vitamin A and Childhood Morbidity: Reports from Clinical Trials** Chair: Dr. Alfred Sommer
1050	Vitamin A Supplementation Reduces Severity of Childhood Illnesses in Ghana Dr. Paul Arthur
1110	Effect of Vitamin A Supplementation on Childhood Morbidity in Northeast Brazil Dr. Mauricio L. Barreto
1130	Impact of High Dose Vitamin A Supplementation on Incidence and Duration of Episodes of Diarrhea and Acute Respiratory Infections in Preschool Indonesian Children Dr. Michael J. Dibley
1150	Discussion and announcements
1230	Lunch

Wednesday, 10 March 1993 (continued)

1400	**Poster sessions** with presenters available: **Consequences for Human Health and Development of Vitamin A Deficiency** **Newer Methodologies for Assessing Subclinical Vitamin A Deficiency**
1445	**Special Presentations on Vitamin A Distribution** Chair: Dr. Aaron Lechtig
1445	Vitamin A Deficiency in Infancy Dr. Barbara A. Underwood
1455	Safety of Vitamin A Supplementation Through EPI in Bangladesh Dr. Andres de Francisco
1505	Delivering Vitamin A Supplements at Immunization Contacts Dr. Nicholas Cohen
1515	Prerequisites for the Initiation of "Universal" VAC Distribution: A Policy Think Piece Dr. Ted Greiner
1530	Discussion
1550	Break
1620	**Newer Methodologies for Assessing Subclinical Vitamin A Deficiency** Chair: Dr. James A. Olson
1620	Indicators of Vitamin A Status: An Overview Dr. James A. Olson
1635	Issues of Using Dietary Methods of Assessment for Vitamin A Deficiency Dr. S. Ismail
1650	Issues Related to Clinical and Histological Methods of Assessment for Vitamin A Deficiency Dr. Alfred Sommer
1705	Issues Related to Biochemical Methods of Assessment for Vitamin A Deficiency Dr. David Ross
1720	**Summary of Consequences for Human Health and Development of Vitamin A Deficiency Poster Session** Dr. Michael Latham
1735	Discussion and announcements
1800	End of day's formal sessions
1900	IVACG Steering Committee dinner and meeting with IVACG Regional Representatives for Africa

Thursday, 11 March 1993

0800-0830	Set up for poster sessions: Dietary Behavior and Surveys
0830-1715	Thursday poster sessions on display, presenters available 1530-1615
0830	**Linking Vitamin A to Other Micronutrient Issues, e.g., Iron and Iodine** Chair: Dr. Anna Verster
0830	Iron Deficiency: The Global Perspective Dr. James Cook
0850	Overview and Update of Iodine Deficiency Dr. Rainer Gutekunst
0910	Panel discussion on Linking Vitamin A to Other Micronutrient Issues, e.g., Iron and Iodine Dr. James Cook Dr. Rainer Gutekunst Dr. Samuel G. Kahn Dr. Frederick Trowbridge
0950	Effects of an Oral Iodine Preparation on the Stability of Retinyl Palmitate Dr. James A. Olson
1005	Role of Vitamin A in Nutritional Anemia: Recent Studies in Pregnant Women in Indonesia, Children in Ethiopia, and in Laboratory Animals Dr. Clive E. West
1020	Discussion
1040	Break
1100	**Agency Commitments for the Virtual Eradication of Vitamin A Deficiency by the Year 2000** Chair: Dr. Suzanne Harris
1100	Food and Agricultural Organization of the United Nations Dr. Franz Simmersbach
1115	UNICEF Mr. David Alnwick
1130	World Health Organization Dr. Barbara A. Underwood
1145	World Bank Mr. James Greene
1200	Administrative Committee on Coordination-Subcommittee on Nutrition (ACC/SCN) Dr. Abraham Horwitz

Thursday, 11 March 1993 (continued)

1215	Discussion and announcements
1230	Lunch
1400	**Agency Commitments for the Virtual Eradication of Vitamin A Deficiency by the Year 2000 (continued)** Chair: Dr. Suzanne Harris
1400	United States Agency for International Development (USAID) Dr. Frances R. Davidson
1415	Swedish International Development Authority (SIDA) Dr. Ted Greiner
1430	United Nations Development Programme, Tanzania Dr. Erick Boateng
1445	Discussion
1530	Break and **Poster Sessions Concerning Dietary Behavior and Surveys** with presenters available
1615	Summaries of Thursday Poster Sessions Chair: Dr. Pawlos Quana'a
1615	**Summary of Dietary Behavior Poster Session** Ms. Suttilak Smitasiri
1630	**Summary of Survey Poster Session** Dr. Rodolfo Florentino
1645	Discussion and announcements
1715	End of day's sessions at AICC
1900-2030	**Video presentations** at Novotel Mt. Meru Hotel Chair: Ms. Ann Burgess

Friday, 12 March 1993

0830	**Nongovernmental Organization Commitments for the Virtual Eradication of Vitamin A Deficiency by the Year 2000** Chair: Dr. Martin Bloem
0830	International Eye Foundation Mr. John Barrows
0840	Sight Savers Mr. Peter Dixon
0850	Eye Care—PROVAX Dr. Alix Fleury
0900	Helen Keller International Dr. Joseph Sclafani
0910	Prevention of Vitamin A Deficiency Through Breastfeeding Promotion: The Role of Wellstart International Prof. Vicky Newman
0920	The Roche SIGHT AND LIFE Task Force: Reflections on Past and Future Activities Dr. John Gmünder
0930	Asian Vegetable Research and Development Center Dr. Romeo Opeña
0940	The Nutrition Foundation, Inc. Ms. Laurie Lindsay Aomari
0950	Discussion
1030	Break
1130	**Future Perspectives on Vitamin A** Chair: Dr. Abraham Horowitz
1130	New Horizons in Vitamin A Research Dr. Frank Chytil
1200	Closing remarks Dr. Abraham Horwitz
1230	End of formal sessions

Saturday, 13 March 1993

Study tours organized by local committee in Tanzania.

- ▲ National Horticultural Research and Training Institute (HORTI Tengeru)
- ▲ World Vision International Area Development Programs in Sanya and Longido
- ▲ UNICEF-sponsored Child Survival and Development Programme in Hai District

Poster and Video Sessions

Monday, 8 March 1993

1515-1600	**Activities for the Control of Vitamin A Deficiency in Tanzania Poster Session** (set up 0800 Monday)
1.	Tengeru Horticultural Activities Mr. R.E.A. Swai
2.	IEC Materials Mrs. Hidaya Missano
3.	Red Palm Oil Mr. G.T. Ndunguru
4.	Diet Modification Mr. L. Mselle
5.	Knowledge, Attitudes, and Practices Study in Shinyanga Mrs. F. Magambo
6.	Solar Drying in Tanzania Mrs. Generose Mulokozi
7.	Solar Drying Vitamin A–Rich Foods Ms. Mary Linehan
8.	Laboratory Support to the National Programme on Vitamin A Deficiency Mrs. Generose Mulokozi and Mr. Claver Temalilwa

Tuesday, 9 March 1993

1515-1600	**Vitamin A Program Issues Poster Session** (set up 0800 Tuesday)
1.	Characteristics of Non-Responsive Bitot's Spots in Nepal Dr. Filippo Curtale
2.	FAO/Australia-Nutrition Improvement Project, Vietnam: A Multisectoral, Community- Based Approach to Addressing Food and Nutrition Problems Dr. Tu Ngu
3.	Relative Protection of One Oral 100,000 IU or 200,000 IU Dose Vitamin A Against Deficiency Dr. Jean Humphrey
4.	Vitamin A Supplementation: A Must During Supplementary Feeding in Refugee Camps in Zimbabwe Prof. N.Z. Nyazema

Tuesday, 9 March 1993 (continued)

5.	Integration of the Delivery of Vitamin A Supplements to Infants and Post-Partum Women into the Routine Immunization Program on Lombok Island, Republic of Indonesia Dr. Augustinus Sutanto
6.	Integration of Vitamin A Capsule Supplementation Into Operation Timbang: A Team Approach Ms. Charito S. Tuason
7.	Evaluation of the National Xerophthalmia Control Program Indonesia 1992 Dr. Muhilal
1515-1600	**New Human Research on the Functions of Vitamin A Poster Session** (set up 0800 Tuesday)
8.	Increased Mortality Associated with Vitamin A Deficiency during HIV Infection Dr. Richard D. Semba
9.	Molecular Mechanisms of Action for Vitamin A-Derived Hormones Dr. Magnus Pfahl

Wednesday, 10 March 1993

1400-1445	**Consequences for Human Health and Development of Vitamin A Deficiency Poster Session** (set up 0800 Wednesday)
1.	The Impact of Vitamin A Supplementation in Preschool Children in Iringa, Tanzania Dr. Godwin D. Ndossi
2.	Effect of Vitamin A Supplementation on Growth and Morbidity of Preschool Children in a Growth Monitoring Research Project in Southern India Mrs. Usha Ramakrishnan
3.	The Relationship Between Vitamin A Status and Severity of Acute Respiratory Tract Infections in Children Dr. Greg Hussey
4.	Effect of a Single Oral Dose of Vitamin A (200,000 IU) on Morbidity in Acute Measles Cases Recruited at Urban Clinics in Ndola, Zambia Dr. Chris Kjolhede
5.	Determinants of Vitamin A Deficiency in Northern Ghana Dr. Saul Morris

Wednesday, 10 March 1993 (continued)

1400-1445	**Newer Methodologies for Assessing Subclinical Vitamin A Deficiency Poster Session** (set up 0800 Wednesday)
6.	Can Community Serum Vitamin A Levels be Used for Predicting the Risk of Xerophthalmia? Ms. Atmarita
7.	Serum Retinol and Acute Phase Proteins of Children in Northern Ghana Dr. Suzanne Filteau
8.	The Stability of Vitamin A Circulating Complex in Spots of Dried Serum Samples Absorbed on Filter Paper Dr. E.M. Kafwembe
9.	Vitamin A Status in Preschool Indonesian Children as Measured by the Modified Relative-Dose Response Assay Dr. Michael J. Dibley
10.	Comparisons of Vitamin A Assessment Techniques in Indonesian Children and Further Refinement of the Modified Relative Dose Response (MRDR) Ms. Sherry Tanumihardjo
11.	Relation Between Impression Cytology Test and Trachoma Dr. Serge Resnikoff
12.	Assessment of Vitamin A Status in China by the Modified Conjunctival Impression Cytology (CIC) Method Dr. Han Ya-shan
13.	A Comparison of Serum Retinol Levels and Conjunctival Impression Cytology Results in Young Children in Ghana Dr. David A. Ross
14.	Assessment of Vitamin A Status by a Prototype Dark Adaptometer Dr. Nathan Congdon
15.	Risk Factors for Xerophthalmia in Nepal Dr. S.K. Khatry
16.	Villages in Transition: Elevated Risk of Micronutrient Deficiency Dr. William D. Drake
17.	Experiences in Training and Use of Modified Versions of the IVACG Simplified Dietary Guidelines Dr. Mohamed Mansour

Wednesday, 10 March 1993 (continued)

18. A Simple Method to Assess Vitamin A Intake: Experience with a Food Frequency Questionnaire for Preschool Children in Rural Central Java, Indonesia
    Mrs. Th. Ninuk S.H.
19. Validation of the HKI Food Frequency Method to Identify Communities with Vitamin A Deficiency
    Dr. Nancy L. Sloan
20. Assessment of the Dietary Intake of Vitamin A by Preschool Indonesian Children by Two Methods
    Dr. Jean Humphrey
21. A Simplified Food Frequency Method to Assess Relative Vitamin A Intake
    Dr. Rebecca J. Stoltzfus

Thursday, 11 March 1993

1530-1615 **Dietary Behavior Poster Session** (set up 0800 Thursday)

1. Production, Vitamin A Content, and Consumer Acceptability of a "Instantized" Sweet Potato Product Prepared in the Form of a Gruel Beverage or Puree Paste: Experience in Guatemala
   Dr. Jesus Bulux
2. Dietary Habits and β-Carotene Rich Food Intakes of Children (6-12 Years of Age) Participating in the Dr. M.G.R. Nutritious Meal Programme
   Dr. Rajammal P. Devadas
3. Assessment of Dietary Behavior Related to Vitamin A in Uganda
   Mrs. Louise Sserunjogi
4. The Impact of Vegetable Variety on Children's Vegetable Consumption in Bangladesh
   Dr. A.K. Tabibul

1530-1615 **Survey Poster Session** (set up 0800 Thursday)

5. Vitamin A Deficiency in the South Pacific: Tuvalu, Vanuatu, Solomon and Cook Islands
   Ms. Mary Linehan
6. The Assessment of Vitamin A Deficiency in Three Cities in Mozambique
   Dr. Manuel L. Romano Julien
7. Kamuli Blindness and Vitamin A Deficiency Survey
   Dr. Medi Kawuma

Thursday, 11 March 1993 (continued)

8.	Vitamin A Deficiency in the Dominican Republic Dr. Hugo R. Mendoza
9.	The Vitamin A Intake of Lactating and Non-lactating Non-pregnant Women in Rural West Java and Local Food Restrictions Which Limit Their Vitamin A Intake Dr. Saskia de Pee
10.	Bolivia Vitamin A Deficiency Prevalence Assessment Dr. David Nelson
11.	The Prevalence of Vitamin A Deficiency and Iron Deficiency Anemia of Preschool Children in Panama Dr. David Nelson
12.	Prevalence of Xerophthalmia and Risk of Vitamin A Deficiency Among Children in the Extreme North Province of Cameroon Mr. Emmanuel Atud Atina
13.	The Implications of Urbanization for Vitamin A Deficiency Amongst Children in South Africa Ms. Anna Coutsoudis

1900-2030	**Video Presentations** at Novotel Mt. Meru Hotel
	Chair: Ms. Ann Burgess
1900	From Darkness Into Light Mr. Nazrul Islam
1920	The Vitamin A Child Survival Project Dr. Filippo Curtale
1940	Ending Hidden Hunger Dr. Aaron Lechtig
2000	Vitamin A and Child Survival Ms. Nancy Haselow

Exhibits

Chair: Dr. Miriam Chavez

Exhibits on display during coffee breaks and poster sessions on Tuesday, Wednesday, Thursday, and Friday.

- ▲ Solar Drying (organized by Tanzania Food and Nutrition Centre and VITAL). This exhibit includes a demonstration of the technique, and shares information from applications in the following countries:
  - —Tanzania—Tanzania Food and Nutrition Centre
  - —Haiti—Save the Children
  - —Dominican Republic—Fundación para el Desarrollo Comunitario, Inc. (FUDECO)
- ▲ The Nutrition Foundation, Inc.
  Dr. Suzanne Harris
- ▲ Tanzania Food and Nutrition Centre
  Mrs. Sylvia F. Shao
- ▲ Vitamin A Assessment Manual
  Ms. Sherry Tanumihardjo and Dr. James Olson
- ▲ Wellstart International
  Prof. Vicky Newman
- ▲ FAO Publications and Vitamin A Activities in Africa
  Dr. Ndiaye Cheikh and Dr. Franz Simmersbach
- ▲ Helen Keller International
  Ms. Nancy Haselow
- ▲ Clearinghouse on Infant Feeding and Maternal Nutrition
  Ms. Man-Ming Hung
- ▲ VITAL
  Ms. Mary Linehan
- ▲ Task Force SIGHT AND LIFE
  Dr. John Gmünder
- ▲ Worldview International Foundation
  Mr. Nazrul Islam
- ▲ Program Against Micronutrient Malnutrition (PAMM)
  Dr. Frederick L. Trowbridge
- ▲ Food and Nutrition Board, Government of India
  Mrs. Shashi Prabha Gupta
- ▲ World Health Organization Micronutrient Deficiency Information System
- ▲ *Xerophthalmia Club Bulletin*
- ▲ International Eye Foundation, Guatemala

Contributors to the XV IVACG Meeting

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Mrs. Martin Solow
Tanzania Tea Blenders
Task Force SIGHT AND LIFE
The World Bank, Tanzania
UNICEF, Tanzania
United Nations Development Programme, Tanzania
World Health Organization, Tanzania

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Appendix 3

XV IVACG MEETING 8–12 MARCH 1993 • ARUSHA, TANZANIA

TOWARD COMPREHENSIVE PROGRAMS TO REDUCE VITAMIN A DEFICIENCY

October 1992

Dear Colleague:

On behalf of the International Vitamin A Consultative Group (IVACG) and the local organizing committee in Tanzania, it is our pleasure to invite you to attend the XV IVACG Meeting in Arusha, Tanzania, 8–12 March 1993 (Monday through Friday). "Toward Comprehensive Programs to Reduce Vitamin A Deficiency" will be the theme of the meeting.

This meeting will include presentations on the main theme as well as oral, poster, and video presentations on related vitamin A program issues. These include experiences in developing and implementing dietary diversification programs, newer methodologies for assessing subclinical vitamin A deficiency, and consequences for human health and development of vitamin A deficiency. The latest research findings on the functions of vitamin A will also be presented. We believe the program will stimulate lively dialogue on these concerns. Further detailed information on the program is contained in this invitation package.

We expect that this meeting will encourage participants to apply new knowledge as well as their experience to the development of sustainable programs for the global eradication of vitamin A deficiency. We look forward to your participation in this important international gathering. Although IVACG cannot offer you travel funds, we hope you will be able to attend the meeting. If you require a personalized invitation to facilitate your travel, please let us know. We anticipate an exciting meeting in Arusha, and believe that your attendance will add to its success.

Best personal regards,

Suzanne S. Harris
Laurie Aomari

Suzanne S. Harris, PhD
Laurie Lindsay Aomari, RD

60

Recent landmark developments have inspired political commitment to the virtual elimination of vitamin A deficiency as a public health problem within the decade. Although the difficulties of reaching this goal are enormous, the progress to date is impressive. Emphasis on moving from small projects to larger, more comprehensive programs and positively using the knowledge of successes and obstacles experienced by colleagues in many countries will build on this progress. Program planning must include operational links to other health and development programs that will support a sustained, adequate vitamin A status for all and especially protect children through the vulnerable early childhood years. Planning must also include evaluations that will allow us to know when we've reached the global goal of eradicating vitamin A deficiency as a public health problem.

XV IVACG MEETING 8–12 MARCH 1993 • ARUSHA, TANZANIA

Policy makers, program managers, planners, and scientists in health, nutrition, biochemistry, agriculture, horticulture, and development are among those who will gather in Tanzania to address the problem of vitamin A deficiency and the many facets of its control. IVACG welcomes participants from international agencies, food and chemical industries, national ministries, educational institutions, and nongovernmental organizations.

PROGRAM OVERVIEW

The XV IVACG Meeting program includes invited presentations and presentations selected from abstracts that represent the collaborative efforts of many individuals and international, bilateral, and nongovernmental organizations. These presentations will challenge participants to reevaluate their assumptions about ways to eliminate vitamin A deficiency. At poster sessions, plenary presentations led by experts from several disciplines, discussion periods, and social events during the meeting, participants will have an opportunity to share perspectives and gain practical insights into these complex issues. English and French will be the official languages for oral presentations during the XV IVACG Meeting. Plenary sessions will take place at the Arusha International Conference Centre. A program will be available after 15 December.

Monday, 8 March 1993

- Meeting inauguration
- National Symposium: Tanzanian colleagues have been leaders in programs to control vitamin A deficiency. Their presentations will focus on programs and accomplishments in Tanzania with a focus on lessons learned that can be applied elsewhere.
- Welcome reception

Tuesday, 9 March 1993

- Projects to Programs: What Does It Take? Keynote speakers will specify the actions needed in several areas to make comprehensive vitamin A programs a reality. Speakers from four countries will respond and share their experiences to make the concepts more tangible.
- Programs: How Do We Know They Are Working? Presenters will highlight evaluation techniques and analysis framework as an essential part of national planning to reach vitamin A program goals.
- Vitamin A program issues will be examined more specifically in oral and poster presentations.

Wednesday, 10 March 1993

- The most recent reports from clinical trials in Ghana, Nepal, Brazil, India, and Indonesia will add to the understanding of the role of vitamin A status in childhood mortality and morbidity.
- Poster Sessions: Consequences for Human Health and Development of Vitamin A Deficiency *and* Newer Methodologies for Assessing Subclinical Vitamin A Deficiency
- Invited presenters will guide participants through the nuances of newer assessment methods and draw attention to poster presentations illustrating current issues.
- World Health Organization colleagues will share updates on important vitamin A activities.

Thursday, 11 March 1993

- Linking Vitamin A to Other Micronutrient Issues, e.g., Iron and Iodine: Oral presentations and a panel discussion will inform participants about the magnitude, etiology, treatment, and prevention of other micronutrient deficiencies and consider coordination of assessment and interventions with vitamin A activities.
- Agency representatives will describe the commitments of United Nations agencies and bilateral agencies for the virtual eradication of vitamin A deficiency by the year 2000.
- Poster Sessions: Dietary Behaviors Influencing Vitamin A Status *and* Recent Vitamin A Surveys
- Colleagues will demonstrate solar drying of vitamin A-rich foods and share new videos used in the control of vitamin A deficiency.

Friday, 12 March 1993

- Nongovernmental organizations will report on their current activities, plans, and commitments that contribute to the eradication of vitamin A deficiency.
- New horizons in vitamin A research will be the focus of a special lecture.
- Closing ceremony

Study Tours

A choice of optional study tours will be offered following the XV IVACG Meeting on Saturday, 13 March, to provide participants an opportunity to learn more about conditions related to vitamin A deficiency in Tanzania. Participants will be responsible for their own expenses during these trips. Approximate costs for transportation and lunch are US$35, payable at registration. All tours described below depart and return from Arusha:

1. **Worldvision International:** During a one-day excursion, groups will visit one of several Worldvision Area Development Programme community projects near Arusha. These projects focus on child survival, agriculture, and education. Each group can accommodate a maximum of 12 visitors.
2. **UNICEF:** Participants in this one-day tour will visit the Child Survival and Development Programme in Hai District. This program emphasizes community action in growth monitoring, sanitation, and education. The program also includes a food-intake project aimed at increasing daily feedings of children through feeding posts and maternal education. This tour can accommodate 40 visitors.
3. **Tengeru Horticultural Research Centre (THRC):** This half-day tour will offer participants an opportunity to tour the scenic horticultural center and learn about seed production, propagation, processing, and preservation of vitamin A-rich foods. THRC will soon be a regional training center for horticulture.

If you plan to attend the meeting and wish to receive further site visit information, please mark the appropriate box on the Meeting Registration Form.

Meeting Materials and Registration

Please complete the enclosed Meeting Registration Form if you plan to attend (or if you cannot attend but wish to receive the meeting summary after the meeting). Send your completed form to the IVACG Secretariat by fax or mail. If you prefer, you can send the necessary information to the secretariat by telex. Please respond by 15 January 1993 so the secretariat staff can prepare your meeting materials. You will receive a brief confirmation of your meeting participation from the IVACG Secretariat.

You can obtain your meeting packet during scheduled on-site registration times. Early registration will be at the Novotel Mt. Meru Hotel on Sunday evening, 7 March. On-site registration will continue on Monday morning, 8 March, at the Arusha International Conference Centre. We encourage early registration for all those who arrive by Sunday evening. Your meeting confirmation will include the specific times for registration.

Exhibits/Videos

The XV IVACG Meeting will provide an opportunity for participants to exhibit materials describing project activities, training and educational opportunities, and private sector initiatives. There will also be a meeting session for showing videos. Space is limited, and prior approval is required in order to show an exhibit or video. If you would like to show an exhibit or video, please return the exhibit/video application form enclosed with this invitation packet to the IVACG Secretariat no later than **15 December 1992**.

Meeting Location

World famous for its natural beauty and wildlife reserves such as the Ngorongoro Crater and Olduvai Gorge, Tanzania offers many opportunities for short-term excursions. Visitors can explore the coastal region and Zanzibar, game parks in the north, or Mt. Kilimanjaro, Africa's highest mountain. Tanzania also offers some of the best opportunities for safaris in East Africa.

Arusha, the meeting venue, has a population of more than 50,000. Located at the foot of Mt. Meru, Arusha serves as the starting point for many safaris, as well as ascents on Mt. Kilimanjaro. The Arusha International Conference Centre, the site of most summit meetings among the East African political community, will serve as the meeting facility.

Participants who wish to participate in a safari should make their own arrangements in advance, or through travel agents in Arusha.

USEFUL INFORMATION

BASIC FACTS

The climate is temperate and should be 75–80°F (23–28°C) during the day and in the 50s in the evenings (16–21°C). Some rain is expected during the time of the meeting. The national languages are Swahili and English. Electricity is 220 volts. The monetary unit is the Tanzanian shilling, although U.S. dollars are required for most hotels and all game park entrance fees. There is also an airport departure tax of US$20 or UK£18, which must be paid in foreign currency.

VISAS

Visas are required of all travelers to Tanzania, except nationals of the Commonwealth countries, Scandinavian countries, Republic of Ireland, Rwanda, Romania, and Sudan. Please check requirements regardless of your nationality and allow adequate time to process the necessary visa(s). For those participants who experience difficulty in obtaining visas, or who wish to enter Tanzania through a border point, please contact the IVACG Secretariat immediately so that we can facilitate your obtaining visas at the border. Participants should carry meeting documents with them during travel.

IMMUNIZATIONS

Malaria prophylaxis is recommended for Tanzania, with mefloquine as the drug of first choice, followed by doxycycline. The U.S. Centers for Disease Control (CDC) recommends yellow fever vaccination, as well as immune serum globulin (gamma globulin) for protection against hepatitis A, particularly if you plan to visit rural areas or areas with poor sanitation. CDC also recommends vaccination for meningococcal meningitis. Those planning extended stays or visits to small cities and rural areas may wish to obtain information regarding prevention of hepatitis B, dengue fever, typhoid fever, rabies, and schistosomiasis. You may wish to have polio and tetanus boosters if you have not had these within the last 10 years.

The XIV IVACG Meeting in Ecuador "was a very useful meeting for mc both in terms of getting informotion and meeting people in this field."

–Dr. Makiko Kinoshita, Japan

"I do not think it is realized by many the several spinoffs that accrue from being at such a meeting . . . All these provide not only a most useful dimension to the work at hand, but also serve as an extremely enriching experience."

–Dr. Saranya Reddy, India

"As a first-time participant I found the meeting very useful and quite exciting."

–Mr. John Barrows, USA

"I was happy about the multidisciplinary representation. We learned quite a lot which we have started to incorporate into our national program."

–Dr. Festo Kavishe, Tanzania

1993 marks the 20th anniversary of the Tanzania Food and Nutrition Centre.

Questions About the Meeting?

Call the IVACG Secretariat
Telephone 202-659-9024
Fax 202-659-3617
Telex 6814107 NUFOUND
Cable NUTRITION WASHINGTONDC

Transportation

International airlines serving Kilimanjaro International Airport (Arusha) and Dar Es Salaam include Ethiopian Air, Air France, KLM and British Airways. Additional airline serve Dar Es Salaam with connections to Arusha on Air Tanzania. Flights and schedule vary widely. Consult your travel agent for information concerning recommended routes and flights. Owing to limited service, we recommend that you make your reservation ea and confirm each international flight more than once between the time of ticket purcha and the day of the flight. For your return flights, travel agents at the conference center will assist with ticket confirmation and schedule changes while you are in Arusha.

The Kilimanjaro International Airport is 40 km from Arusha. Taxi service is available, and fares fluctuate depending on current exchange rates and your negotiating skill.

For those wishing to make connections in Nairobi, Kenya, there is a daily bus that operates between the Norfolk Hotel in Nairobi, Kenya, and the Novotel Mt. Meru Hotel in Arusha, Tanzania. The bus ride takes about five hours and costs 575 Kenyan shillings o way (US$25). This bus can also be taken from Arusha to Nairobi. For more information please contact Mr. George Mathenga of Kesani Tours in Nairobi, Kenya (telephone: 254-2-212804/230140/228241; fax: 254-2-741636).

Hotel Accommodations

The IVACG Secretariat recommends the Novotel Mt. Meru Hotel, the official hotel of the XV IVACG Meeting, for your accommodations during the meeting. Alternativ ly, you m wish to stay at either New Arusha Hotel or Hotel Seventy Seven. All of the hotels are a short distance from the conference center and shuttle service will be available. All three hotels have multilingual staff, on-site travel agencies, one or more restaurants, and extended hours for room service. Novotel Mt. Meru Hotel and New Arusha Hotel have swimming pools.

Room rates and other hotel information are shown on the enclosed chart. You will be responsible for your room charges, meals, and incidental expenses.

Please make your hotel reservation directly with the hotel of your choice no later than 15 January 1993. For your convenience, complete the hotel reservation form included with this invitation and send the information to the hotel by fax or telex. You will receive a hotel confirmation directly from the hotel. If you have questions regarding your reserva tion, please discuss them with the hotel. Please note, due to the popularity of this location cancellation policies are strict.

The Sponsors

Numerous organizations will provide support for participants in the XV IVACG Meeting. The XV IVACG Meeting is sponsored by the Tanzania Food and Nutrition Centre, the National Vitamin A Consultative Group of Tanzania, and IVACG. A committee of Tanzanian professionals concerned with vitamin A deficiency is organizing the national symposium, serves in an advisory capacity to the IVACG Secretariat, and will provide other assistance for the meeting. The IVACG Steering Committee and the IVACG Secretariat are planning and organizing the remainder of the IVACG meeting through a cooperative agreement between the Office of Nutrition, Bureau for Research and Development, U.S. Agency for International Development and The Nutrition Foundation, Inc.

IVACG

The International Vitamin A Consultative Group was established in 1975 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 seek to reduce vitamin A deficiency. As part of this service, IVACG has prepared a series of state-of-the-art scientific guidelines and recommendations available through its publications program. Through its international meetings, IVACG provides a forum to foster the interchange of ideas, the presentation of new research findings and survey data, and discussion of action programs.

XV IVACG MEETING HOTEL INFORMATION AND RESERVATION FORM

8-12 MARCH • ARUSHA, TANZANIA **RESERVATION DEADLINE • 15 JANUARY 1993**

INFORMATION	NOVOTEL MT. MERU HOTEL	HOTEL SEVENTY SEVEN	NEW ARUSHA HOTEL
Single (includes tax, service, breakfast)	US$47	US$41.50	Not available
Double (includes tax, service, breakfast)	US$59	US$51.50	US$60
Suite (includes tax, service, breakfast)	Junior suite US$65 Presidential suite US$80	Executive room US$62 Suite US$104	None
Deposit required to guarantee room	Two nights' room rate by credit card, foreign currency bank draft or international money order (see below*)	Two nights' room rate by foreign currency bank draft or international money order (see below*)	
Payment Method	American Express, MasterCard, Visa, Diners Club, Eurocard, or foreign currency travelers checks	Credit cards not accepted. Payment must be made in foreign currency or foreign currency travelers checks.	
	* Foreign currencies accepted: US dollars, British pounds, Canadian dollars, Deutsch marks, French francs, Swiss francs		
Refund/Cancellation Policy (All cancellations and changes must be made in writing.)	Full refund if written notice is received 30 days prior to arrival. Deposit will be forfeit if cancellation is received less than 30 days prior to arrival or no show.	Full refund if written notice is received 35 days prior to arrival; 35% per day charged for cancellation between 35 days and 48 hours prior to arrival; 75% per day charged for cancellation within 48 hours of arrival or no shaw.	Full refund if written notice is received 7 days prior to arrival; 75% charged if notice is received less than 7 days prior to arrival for cancellation or no show.
Send reservations to attention of...	Front Office Manager	General Manager	General Manager
Telephone	255-57-2711 or 8500	255-57-3800	255-57-3241
Fax	255-57-8221	255-57-8405	255-57-8085
Telex	42065	42055 Cable: SEVTEL TZ	42034 Telegrams: "Centre" Arusha
Address	PO Box 877, Moshi Road Arusha, Tanzania	PO Box 1184 Arusha, Tanzania	PO Box 88, Boma Road Arusha, Tanzania

All room rates are quoted in US dollars. Tanzania residents' rates may be different and are payable in Tanzanian shillings.

KEEP TOP PORTION. SEND BOTTOM PORTION TO HOTEL OF YOUR CHOICE.

HOTEL RESERVATION FORM ▲ XV IVACG MEETING

Please complete the form below. Send this information and your deposit directly to the hotel of your choice no later than 15 January 1993. The address for each hotel is shown in the chart above.

Name _____ Organization _____

Address _____

_____

Telephone _____ Fax _____ Telex _____

I need a ☐ single room ☐ double room ☐ suite. If sharing a room please provide roommate's name _____

Arrival Date/Time _____ Airport _____ Airline and flight _____

Departure Date/Time _____ Airport _____ Airline and flight _____

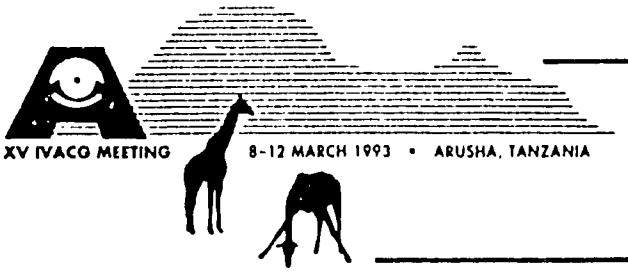
Deposit required. Please guarantee my room using the enclosed

☐ foreign currency bank draft ☐ international money order ☐ credit card number (Novotel Mt. Meru Hotel only)

Credit Card Type _____ Card Number _____

Expiration Date _____ Signature _____

☐ Please send me a confirmation of my reservation.



XV IVACG MEETING REGISTRATION FORM

IVACG Secretariat ▲ The Nutrition Foundation, Inc.
1126 Sixteenth Street, NW ▲ Washington, DC 20036 USA
Telephone 202-659-9024 ▲ Fax 202-659-3617
Telex 6814107 NUFOUND

Please answer all items and return this information to the secretariat by mail, telephone, fax, or telex as soon as possible.
Your response must be received by 15 January 1993.

COMMUNICATIONS INFORMATION

Dr Prof Ms Mrs Mr First Name _____ Family Name _____

Job Title/Position _____

Organization _____

Mailing Address _____

_____

Telephone _____ Fax _____

Telex _____ Alternative Fax _____

NAME BADGE INFORMATION

Please enter the information as you wish it to appear on your name badge. Indicate preference (check one):

Dr Prof Ms Mrs Mr

Name _____

Organization _____

_____

ATTENDANCE

I will attend

I will not attend but wish to receive the meeting summary.

I made my hotel reservation at Novotel Mt. Meru Hotel

Hotel Seventy Seven New Arusha Hotel

Other _____

Arrival Airport _____

Arrival Date/Flight _____

Departure Airport _____

Departure Date/Flight _____

STUDY TOURS

Please register me for one of the following tours:

UNICEF Worldvision Tengeru

Please send me more information about the following tours:

UNICEF Worldvision Tengeru

INVITED SPEAKERS ONLY

I accept your invitation to give a presentation.

I will need a slide projector overhead projector.

I am unable to accept your invitation to give a presentation.

EXHIBIT/VIDEO APPLICATION

If your organization wishes to bring exhibit materials or a video, please complete and return this form to the IVACG Secretariat. Exhibits or videos require prior approval through the IVACG Secretariat. The secretariat will inform presenters whose exhibit or video is accepted.

I wish to bring materials for exhibit a video to the XV IVACG Meeting.

Presenter's Name: _____

Description of materials for exhibit or video content: _____

_____

_____

Title of video: _____

Length of video: _____ Format (please circle): VHS PAL/SECAM

Appendix 4

IVACG Group

Chairman
Dr. Abraham Horwitz, PAHO/WHO

Secretary
Dr. Frances R. Davidson, USAID

Secretariat:
The Nutrition Foundation, Inc
1126 Sixteenth St., N.W.
Washington, D.C. 20036
Cable: NUTRITION WASHINGTONDC
Telex: 6814107 "NUFOUND"
Phone: (202) 659-9024
Facsimile: (202) 659-3617

COMPREHENSIVE VITAMIN A PROGRAMS WERE FOCUS OF RECENT XV IVACG MEETING

For Immediate Release
Contact: Laurie Lindsay Aomari, R.D.
(202) 659-9024

Washington, D.C. -- Integration of vitamin A interventions into existing primary health care and food-based strategies unites commitment with action, according to participants at the recent XV IVACG Meeting in Tanzania. "We must seize the global momentum to virtually eliminate vitamin A deficiency and enact comprehensive, coordinated measures to prevent vitamin A deficiency," said Dr. Abraham Horwitz, chairman of the International Vitamin A Consultative Group (IVACG) as he opened the XV IVACG Meeting.

Representatives from 51 countries were among the 294 policy makers, implementors, and scientists in health, nutrition, agriculture, and development participating in the meeting, held 8-12 March 1993 in Arusha, Tanzania. Throughout the five-day program numerous speakers presented research concerning progress in changing dietary behaviors related to vitamin A, newer methodologies for assessing subclinical vitamin A deficiency, consequences for human health and disease, and physiological functions of vitamin A.

Several speakers presented evidence of substantial gains in meeting the goal of virtual eradication of vitamin A deficiency. A significant outcome is the reduction in childhood mortality from infections. The impact of vitamin A supplementation on mortality appears to be due to a reduction in the severity of infection rather than in the incidence of infection.

Others referred to "missed opportunities" in linking vitamin A with health care delivery systems such as immunization services and growth-monitoring programs. These are the "windows of opportunity" for the future.

- more -

A comprehensive approach to preventing vitamin A deficiency combines short-term strategies such as vitamin A capsule distribution with dietary diversification, a long-term strategy. Factors identified as essential for a successful vitamin A program include adequate political will; effective surveillance to guide policy formulation, program design, and implementation; and flexible training, supervision, and management systems.

In closing the meeting, Dr. Horwitz stated, "The reduction of poverty, although essential, is not a prerequisite for the elimination of vitamin A deficiency. The process to reach this goal should start or be strengthened, and the sooner the better. The persistence of vitamin A deficiency anywhere in the world is cruel, because it exposes mothers and children to great risks. It is immoral, because it ignores basic human values. It is unacceptable, because it can be prevented."

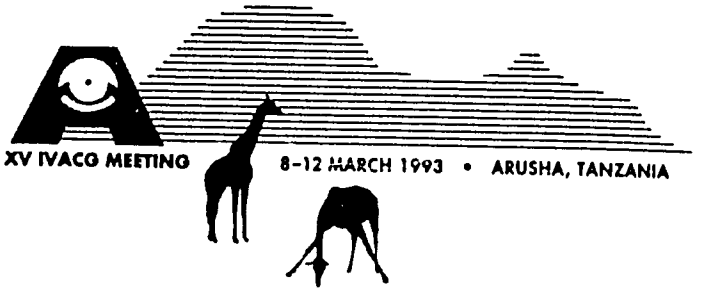
A complete report of the meeting will be available from the IVACG Secretariat, 1126 Sixteenth Street N.W., Washington, D.C. 20036, USA.

With support from a cooperative agreement between the Nutrition Foundation, Inc. and the Office of Nutrition, Bureau for Research and Development, U.S. Agency for International Development, the IVACG Steering Committee and Secretariat organized the meeting with a local committee in Tanzania. Other organizations, including bilateral agencies, United Nations agencies, and the food industry, provided additional support.

IVACG was established in 1975 to guide international activities aimed at reducing vitamin A deficiency in the world. IVACG strongly supports the goal of virtually eliminating vitamin A deficiency by the turn of the century. The XV IVACG Meeting provided a forum for exchanging new ideas and important research findings, encouraging innovation, and promoting action programs to help reach the goal.

# # #

Appendix 5



Toward Comprehensive Programs to Reduce Vitamin A Deficiency

XV International Vitamin A
Consultative Group Meeting

Arusha, Tanzania
8–12 March 1993

Table of Contents

Appendix 6

International
Vitamin A
Consultative
IVACG Group

Chairman
Dr Abraham Horwitz, PAHO/WHO

Secretary
Dr Frances R Davidson, USAID

Secretariat
The Nutrition Foundation, Inc
1126 Sixteenth St, N W
Washington D C 20036
Cable NUTRITION WASHINGTONDC
Telex 6814107 "NUFOUND"
Phone (202) 659-9024
Facsimile (202) 659-3617

Minutes of the IVACG Steering Committee Meetings
9 and 10 March 1993
Arusha, Tanzania

Participants: Dr. Moses C. Chirambo, Dr. Frances R. Davidson, Dr. Suzanne S. Harris, Dr. Abraham Horwitz, Dr. Vinodini Reddy, Dr. Leonor Maria P. Santos, Dr. Franz Simmersbach, Ms. Suttilak Smitasiri, Dr. Alfred Sommer, Dr. Barbara A. Underwood, Dr. Keith P. West, Ms. Laurie Aomari. Dr. Festo P. Kavishe and Dr. Pawlos Quana'a joined the meeting on 10 March for the discussion concerning activities of the IVACG regional representatives for Africa.

These meetings were held on two evenings during the XV IVACG Meeting. As chair of the IVACG Steering Committee, Dr. Underwood opened the meeting on 9 March 1993 at 1955 and invited Dr. Horwitz to give opening remarks. Dr. Horwitz expressed pleasure with the XV IVACG Meeting organization and the cooperation of the coordinating committee. He commended Tanzania for a rational program to prevent and control vitamin A deficiency. Dr. Horwitz also welcomed Ms. Smitasiri and Dr. West as new members of the IVACG Steering Committee and invited their important contributions for IVACG's future. Dr. Underwood also welcomed the new members' participation and commended the secretariat regarding the organization of the XV IVACG Meeting.

XV IVACG Meeting

Several changes to the meeting program were discussed. Dr. Underwood noted a request from WHO Control of Diarrheal and Respiratory Diseases Division (CDR) to present a summary of the results of the Acute Respiratory Infection (ARI) meeting to review the meta analysis of vitamin A supplementation and childhood pneumonia held in Geneva in early February. The final report has not been reviewed by those who attended the deliberations. Dr. Sommer agreed to simply announce that the meeting occurred, that a meta analysis is underway, and that the report will be available. Dr. Horwitz stated his support of Dr. Sommer's idea and further suggested that a letter be prepared on behalf of the IVACG Steering Committee to send to CDR in Geneva.

For future IVACG meetings, Dr. Simmersbach recommended that IVACG encourage scientists to carry out more research in areas such as nutrition education and program sustainability. Dr. Horwitz noted the importance of building on the theme of the XV IVACG Meeting for the next IVACG meeting in order to continue moving toward the goals to which governments have committed themselves. Dr. Underwood encouraged early announcement of the meeting theme in order to inspire presentations from several groups working on dietary diversification projects.

Publications Update

Ms. Aomari stated that *Nutrition Communications in Vitamin A Programs: A Resource Book* has been distributed and that kudos and many inquiries are still arriving at the secretariat, including a request from editors of *Journal of Nutrition Education* to review the book. Dr. Underwood stated that the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) wants to use the book as a model. The group agreed that the secretariat should develop a plan and budget for translating the book into French and Spanish. This proposal could then be forwarded to other organizations for financial support, e.g., FAO, AID, Task Force Sight and Life, and the Micronutrients Initiative.

Ms. Aomari reported that "A Brief Guide to Current Methods of Assessing Vitamin A Status" will be published this spring. Dr. Sommer mentioned that the information will go out of date quickly and that this should be considered while making printing decisions.

In a recent letter to Ms. Aomari, Dr. McLaren expressed his intent to drop the word "club" from *Xerophthalmia Club Bulletin*. The steering committee was not in favor of this because this word implies that subscribers are part of a group and that they can contribute to the publication. Additionally, some felt omission of the word puts too much emphasis on the word xerophthalmia as opposed to other dimensions of vitamin A deficiency. Based on this discussion, Ms. Aomari will write to Dr. McLaren. The members did not oppose Dr. McLaren's wish to omit the title secretary from his byline. In future issues only his role as editor will be mentioned.

Some members felt the editor of *Xerophthalmia Club Bulletin* should receive some support for attending the next IVACG meeting in order to facilitate the inclusion of meeting information in the *Bulletin*. The committee recommended that abstracts of the following XV IVACG Meeting presentations be forwarded to Dr. McLaren for inclusion in the next issue:

- Evaluation of a Policy of Routine High Dose Vitamin A Therapy for Children Hospitalized with Measles--presented by Dr. Greg Hussey

- Vitamin A Status and Lactation in Indonesian Women: A Randomized Trial of High-Dose Supplementation in the Post-Partum Period--presented by Dr. Rebecca Stoltzfus

- Effectiveness of Vitamin A Supplementation in Control of Young Child Morbidity and Mortality in Developing Countries--presented by Dr. George Beaton

Dr. Underwood recommended that the committee consider revising *Vitamin A*

Supplements: A Guide to Their Use in the Treatment and Prevention of Vitamin A Deficiency and Xerophthalmia.

The committee discussed revision of *Guidelines for the Development of a Simplified Dietary Assessment to Identify Groups at Risk for Inadequate Intake of Vitamin A*. A revision could take several forms based on the variety of experiences with this and related methods. After discussion, the group agreed that Dr. West would chair a task force to review the strengths and limitations of *Guidelines for the Development of A Simplified Dietary Assessment to Identify Groups at Risk for Inadequate Intake of Vitamin A* and make recommendations for strengthening the method and other dietary assessment methods for vitamin A intake. Dr. West will develop a list of candidates for the task force and draft the terms of reference for consideration by the steering committee.

Dr. Underwood described recent developments related to vitamin A distribution through immunization programs. The draft document on this topic was presented to the WHO Expanded Programme on Immunization (EPI) in October 1992 but no action was requested pending a meta analysis of the morbidity data related to vitamin A supplements and acute lower respiratory infection. CDR convened a meeting in early February to discuss the meta analysis. A report of this meeting is being prepared.

Since the meta analysis has been completed, the WHO Nutrition Unit plans to complete the document prepared by IVACG and EPI on vitamin A distribution through immunization programs as a report of the meeting held 30 June-1 July 1992. Dr. Underwood said that the IVACG Steering Committee will have an opportunity to review the document before it is released by the Nutrition Unit.

IVACG Steering Committee Chair

Dr. Underwood resigned as chair of the IVACG Steering Committee. She encouraged those present to select a new chair from among the current steering committee members in accord with the guidelines given to the steering committee when it was formed. Dr. Horwitz commended Dr. Underwood on the significant experience, knowledge, and leadership that she has contributed to the IVACG Steering Committee. He requested that she serve as chair for the remaining steering committee meeting and that the selection of a new chair not be made until after the discussions concerning future activities at that meeting. Dr. Sommer seconded these remarks and added his appreciation for Dr. Underwood's devotion and efforts to expand IVACG's role.

Dr. Underwood closed the meeting at approximately 2130 on 9 March 1993.

Dr. Underwood opened the meeting on 10 March 1993 at 1750 and welcomed Dr. Quana'a and Dr. Kavishe.

IVACG Regional Representatives for Africa

The IVACG Regional Representatives for Africa were invited to summarize their recent activities and suggestions during this steering committee meeting. Due to illness, Dr. Diallo was unable to attend the XV IVACG Meeting and this steering committee meeting.

Dr. Quana'a reported that the current political situation in Ethiopia has made assessment of nutritional status outside of Addis Ababa extremely difficult. Malnutrition and hypovitaminosis A is rampant among the displaced population now in Addis Ababa and vitamin A capsule distribution is underway. Relief efforts are being organized.

Dr. Kavishe reminded the committee of the Tanzanian vitamin A activities that were summarized during the first day of the XV IVACG Meeting. He has been able to visit Zambia to assist with a national task force and national plan for vitamin A, and he has collaborated with the Tropical Diseases Research Centre library. Dr. Kavishe is assisting with a survey in Zimbabwe, taught in a course there recently, and is participating in discussions concerning their proposed national program. Dr. Kavishe recommended additional support for Uganda and Namibia.

Dr. Kavishe was instrumental in drafting the micronutrient section of the nutrition strategy for Africa being prepared by the Organization on African Unity. Nongovernmental organizations in the region keep him informed of their activities. When Dr. Kavishe has business in a nearby country, he tries to also use this as an opportunity to promote IVACG.

Dr. Kavishe has received publications requests from Zaire and has been able to distribute IVACG publications to professionals in the countries of his region. Dr. Kavishe commented that IVACG publications are particularly helpful to his work in the region. He noted that African countries are requesting a guide for how to initiate vitamin A programs. If there is a task force on this topic, he suggested that it include those who have experience in programs and in information, education, and communication; and those who have strong scientific knowledge concerning vitamin A deficiency. Training individuals in vitamin A and other micronutrients will also be useful and this is being considered with assistance from the Program Against Micronutrient Malnutrition (PAMM).

Dr. Underwood recommended that, where possible, the regional representatives should also coordinate with committees for blindness prevention.

Future Activities

At the request of Dr. Underwood, Dr. Simmersbach chaired this part of the meeting. Dr. Simmersbach summarized several points from a document prepared earlier for steering committee consideration: "Strategic Placement of IVACG in the Evolving Micronutrient Field." Dr. Simmersbach asked members to comment regarding the following points:

1. What should be IVACG's new tasks and research agendas?
2. What strategies should IVACG take to achieve its future goals?
3. What are the administrative and structural consequences of these strategies?
4. What is the next step for the document "Strategic Placement of IVACG in the Evolving Micronutrient Field?"

Dr. Chirambo suggested that IVACG need not change dramatically but that it should strive to avoid duplication with other groups. Dr. Horwitz said that he would prefer to finalize the document on strategic placement but that it should be more focussed; he implied that the discussion should look to the next ten to 20 years. Dr. Sommer noted that IVACG has been effective since it does more than just organize international meetings.

Dr. Reddy recommended that IVACG remain focussed on vitamin A rather than expand to other micronutrients; meanwhile, IVACG should work collaboratively with other micronutrient groups. Despite IVACG's success in the past, she encouraged a shift in emphasis. Dr. West agreed that IVACG should remain focussed on vitamin A while networking with ICCIDD and the International Nutritional Anemia Consultative Group (INACG). Dr. Horwitz voiced support for a shift in emphasis.

Dr. Simmersbach suggested that the new emphasis could include new research areas. Ms. Smitasiri noted IVACG's efforts to raise awareness of policy makers and scientists regarding vitamin A deficiency; she recommended that the focus now be on assisting action that fosters achievement of the vitamin A goals for the year 2000. Dr. Reddy commented on the need to define measurable vitamin A goals for the year 2000.

Dr. Simmersbach stressed the need for IVACG to be prominent and said that to be prominent, IVACG has to provide the technical tools and criteria to reach the year 2000 goals. He stated that IVACG should continue to give in-depth attention to the issues. Dr. Reddy pointed out that IVACG can also have joint consultations when that seems appropriate.

Dr. Sommer suggested that IVACG should choose several important topics related to vitamin A deficiency that could each be studied by a task force. Assessment, morbidity and mortality, and toxicity of vitamin A supplements were potential topics

mentioned. The results of each task force's deliberations could be presented with policy implications at the next IVACG meeting. Dr. Simmersbach cited dietary assessment as another important topic. Dr. Horwitz voiced the need to define criteria for changing emphasis from the short-term intervention of vitamin A supplementation to long-term dietary interventions. He also mentioned the following topics for IVACG consideration: training criteria, operations research, and how to make interventions more cost effective. Dr. Simmersbach observed that future task forces should provide visible, authoritative, and scientific recommendations.

The group next considered whether implementing such task forces would require administrative and structural changes. Dr. Simmersbach questioned whether reliance on one donor, AID, was sufficient support. Dr. Sommer asked how much AID is willing to support. Dr. Davidson responded that the secretariat develops a negotiable work plan and budget. Dr. Horwitz endorsed having core support from AID but recommended that proposals could be developed for specific activities that might then be supported by other donors. Dr. Underwood indicated that additional donors might wish to participate in an executive committee.

Dr. Simmersbach noted that a mission statement would be helpful in seeking the support of other donors. Dr. Sommer read the two draft mission statements below:

- To improve the vitamin A status of deficient populations so as to eliminate its consequences by stimulating and disseminating relevant research, formulating appropriate policy implications, and advocating for their implementation.

- IVACG is devoted to stimulating and disseminating research, identifying policy implications, and advocating their implementation relevant to understanding and eliminating the consequences of vitamin A deficiency.

Dr. Underwood remarked on IVACG's need for designated experts that the agencies can call upon. Dr. Horwitz stated that the steering committee can appoint committees as needed or requested by the agencies. Dr. Sommer proposed that a list of experts could be called upon for task force participation.

By 1 May Dr. Simmersbach will draft a document that includes ideas generated from this discussion. The IVACG Secretariat will send this document to all steering committee members and request that they return their comments within two weeks.

Ideas for the XVI IVACG Meeting

Dr. Underwood conveyed a suggestion that Thailand be the site for the XVI IVACG Meeting. Vietnam and China were also suggested but the committee preferred Thailand. Ms. Smitasiri encouraged the committee to consider the outcome desired from the meeting and then choose a site within the country that is supportive of that

action. Dr. Underwood asked the secretariat to investigate potential sites in Thailand.

The steering committee has not received an official invitation from the government of Thailand. However, a letter was received from colleagues at the Institute of Nutrition of Mahidol University. The committee agreed that Dr. Horwitz could announce that an invitation was received and that it needs to be confirmed.

Several members made the following suggestions about the meeting:

1. Policy issues should be included.
2. Sound papers developed on important topics could be presented.
3. The content should build on themes of recent IVACG meetings.
4. A short course could cover the repeated themes needed for program implementation.
5. A one-day course could be offered for policy makers.
6. The content and organization of the meeting should be able to accommodate a diverse group of about 300 participants.

Other Business

Dr. Davidson announced that representatives of IVACG, INACG, and ICCIDD met to consider joint efforts between the groups. Based on their deliberations, a team will go to the Philippines to assess joint activities for micronutrients. Members of the team are Dr. Abraham Horwitz, Dr. Keith West, Dr. James Cook, and Dr. John Dunn.

Dr. Underwood closed the meeting at 2250 on 10 March 1993.

Signed: Laurie Lindsay Aomari

Laurie Lindsay Aomari, RD
IVACG Secretariat

Date: 18 May 1993

Appendix 7

WHO/NUT/EPI/93.1
Distr.: Limited
English only

Using Immunization Contacts to Combat Vitamin A Deficiency

Report of an informal consultation

World Health Organization, Geneva

30 June - 1 July 1992

WHO
Nutrition Unit
Expanded Programme on Immunization

and

The International Vitamin A Consultative Group (IVACG)

Table of Contents

Appendix 8

A Brief Guide to Current Methods of Assessing Vitamin A Status

A REPORT OF THE INTERNATIONAL VITAMIN A CONSULTATIVE GROUP (IVACG)

Table of Contents

IVACG

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Vitamin A
Consultative
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IVACG RELEASES
A BRIEF GUIDE TO CURRENT METHODS OF ASSESSING VITAMIN A STATUS

For Immediate Release
Contact: Laurie Lindsay Aomari, RD
(202) 659-9024

Washington, D.C. -- A Brief Guide to Current Methods of Assessing Vitamin A Status is the newest in a series of monographs published by the International Vitamin A Consultative Group (IVACG). This book is an introduction to various current dietary, physiological, biochemical, histological, and clinical procedures for the assessment of vitamin A deficiency. Investigators and program planners will find the text helpful in selecting assessment methodologies best suited to their specific situations and available resources.

Each chapter includes a brief description of a procedure, a discussion of its advantages and limitations, information about interpretation of the data obtained from the method, and an example of its application. Key recent references for each procedure aid the reader in gathering more detailed information. An IVACG task force of scientists from several nations contributed to the development of this new monograph. Dr. Barbara A. Underwood and Dr. James A. Olson served as the book's editors.

Single copies of this and other IVACG publications are available free of charge to representatives in developing countries and for US$3.50 to those in other nations. Order copies from the IVACG Secretariat, The Nutrition Foundation, Inc., 1126 Sixteenth Street, N.W., Washington, D.C. 20036, USA. Please make checks payable in U.S. dollars to The Nutrition Foundation.

A cooperative agreement between The Nutrition Foundation and the Office of Nutrition, Bureau for Research and Development, U.S. Agency for International Development provided major support for this publication. The International Vitamin A Consultative Group was established in 1975 to guide international activities for reducing vitamin A deficiency in the world.

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Appendix 9

NUTRITION COMMUNICATIONS IN VITAMIN A PROGRAMS

A RESOURCE BOOK

International Vitamin A Consultative Group (IVACG)

Contents

A C G

International
Vitamin A
Consultative
Group

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New from IVACG
NUTRITION COMMUNICATIONS IN VITAMIN A PROGRAMS: A RESOURCE BOOK

For Immediate Release
Contact: Laurie Lindsay Aomari, R.D.
(202) 659-9024

Washington, D.C. -- The International Vitamin A Consultative Group (IVACG) breaks new ground with its latest publication, now available from the IVACG Secretariat. *Nutrition Communications in Vitamin A Programs: A Resource Book* uses many examples and full-color photographs in presenting experiences, facts, and visual and textual information to inspire creativity and action in those who combat vitamin A deficiency in the field.

Nutrition education and communications can contribute to the control, prevention, and elimination of vitamin A deficiency as a direct intervention in its own right and by enhancing and reinforcing all other interventions. This richly illustrated book will be a valuable resource to nutritionists and communications experts as they plan nutrition communications activities within larger, ongoing vitamin A programs. Although the book emphasizes vitamin A deficiency, the concepts and techniques presented are relevant to other health and nutrition issues.

The book summarizes the basic methodological issues associated with planning, developing, and implementing nutrition communications activities. The main part of the book describes and gives examples of communications activities and their associated creative materials, provides a list of recommended readings, and outlines successful efforts undertaken in seven countries: Bangladesh, Brazil, India, Indonesia, Mauritania, Nepal, and Thailand. Color photographs of printed materials and field activities plus English translations of scripts from radio and television spots are included.

- more-

Single copies of this and other IVACG publications are available free of charge to representatives in developing countries and for US$3.50 to those in other nations. Order copies from the IVACG Secretariat, The Nutrition Foundation, Inc., 1126 Sixteenth Street, N.W., Washington, D.C. 20036, USA. Please make checks payable in U.S. dollars to The Nutrition Foundation.

Colleagues and organizations around the world contributed to the development of this resource book. The text reflects these contributions as well as the collective experiences of IVACG task force members and the critiques of several reviewers.

A cooperative agreement between the Office of Nutrition, Bureau for Research and Development, U.S. Agency for International Development and The Nutrition Foundation provided major support for this publication. The International Vitamin A Consultative Group was established in 1975 to guide international activities for reducing vitamin A deficiency in the world.

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Appendix 10

XEROPHTHALMIA CLUB

BULLETIN 51

NOVEMBER 1992

Supported by Sight Savers (Royal Commonwealth Society for the Blind) and the International Vitamin A Consultative Group

Bulletins are *sent free* to anyone seriously concerned with xerophthalmia
Please apply for membership to the Club Secretary

ARUSHA, TANZANIA – THE SITE FOR MARCH IVACG MEETING

"Toward Comprehensive Programs to Reduce Vitamin A Deficiency" will be the theme of the XV International Vitamin A Consultative Group (IVACG) Meeting, 8-12 March 1993, in Arusha, Tanzania. The meeting will begin with a national symposium focussing on programs and accomplishments in Tanzania. Following this, the meeting will feature invited presentations on the meeting theme as well as oral, poster, and video presentations on the following:

- Vitamin A program issues (e.g. costs, management or integration with other programs)
- Progress in changing dietary behaviors related to vitamin A
- Newer methodologies for assessing subclinical vitamin A deficiency
- Consequences for human health and development of vitamin A deficiency
- New human research related to the functions of vitamin A.

Through its international meetings, IVACG provides a forum for new ideas, encourages innovations, recognises important research findings, increases awareness of the latest survey data, and promotes action programs. The published conclusions of these meetings reflect the perspectives of those addressing vitamin A issues in varied settings.

IVACG welcomes to its meetings participants from international agencies, national ministries, educational institutions, and non-governmental organizations. Among the 200 participants expected to attend the XV IVACG Meeting are policy makers, programmers, and scientists in health, nutrition, agriculture, horticulture, and development.

The XV IVACG Meeting is sponsored by the Tanzania Food and Nutrition Centre, the National Vitamin A Consultative Group of Tanzania, the International Vitamin A Consultative Group (receiving funding through a cooperative agreement with the US Agency for International Development), and others.

To receive more information about the meeting, write or call the IVACG Secretariat, The Nutrition Foundation, Inc., 1126 Sixteenth Street, N.W., Washington, D.C. 20036, USA. The secretariat telephone number is (202) 659-9024; the secretariat fax number is (202) 659-3617.

The International Vitamin A Consultative Group was established in 1975 to guide international activities for reducing vitamin A deficiency in the world.

CICELY WILLIAMS

Few readers of this Bulletin will not have heard of this redouhtable woman doctor, the first to serve in the British colonial medical service, and described as the doyenne of child nutrition and founder of tropical child health. Cicely died on July 13 at the great age of 98. Until a few years ago and for long after retirement, as before it, she never ceased to espouse the cause of deprived and sick children everywhere, in her writings, lectures, correspondence and conversation on every possible occasion.

Her classical description of kwashiorkor in Ghana in the early 1930s eventually brought her worldwide recognition and honour. It was her impassioned pleas for realism and kindness at the bedside and in the clinic that transfixed and fascinated generations of students and colleagues. For one who was privileged to work with her over several years in London and Beirut and to have had Cicely as a close friend of the family thereafter her inspiration will not fade. Like other rare 'characters' she had many memorable sayings, such as – 'the gut in malnutrition is not paper thin; it is tissue paper thin', and of a colleague who felt he had received a snub, as many do, when he received a lesser decoration than he expected, one that would not permit him to be addressed as 'Sir', Cicely quipped – 'a bad case of knighthood starvation' – a reference to the nightcap drink that claimed to prevent 'night starvation'! Her own CMG was late in being awarded and yet years before she was being feted around the world, especially in the United States. Cicely's full and adventurous life, including her captivity in Singapore during the war, has been told more than once.

It is sad to realise that within a few rnonths of each other we have lost both Cicely and her dear friend Dick Jelliffe (see Bulletin no. 50). It is good to learn that Dick will receive, posthumously, a Lifetime Achievement Award from the International Health Section of the American Public Health Association in November. What may one ask is being planned to honour the memory of the greatest woman in the maternal and child health field?

Donald S McLaren

XEROPHTHALMIA AROUND THE WORLD

AMONG THE NAVAJO

When I am engaged in helping to despatch the bulletins to their destinations I often try to picture what the postman sees; and wonder whether you are still out there at the end of the line: not always evidently! An ophthalmologist, Dr Clyde Farson wrote recently from Alaska to say that in 1981 he had left Tuba City, Arizona where he had been working on a Navajo Indian Reservation. He had not thought of continuing to receive the bulletin when he moved to Alaska but somehow our last issue reached him from 'a kindly postmaster' in Tuba City!

Dr Farson goes on to say how in 1977 after several years of drought he saw several Navajo children with corneal xerophthalmia. The Navajo sheep and the Hopi cattle were found by staff from the University of Arizona to have very low blood levels of vitamin A and some of the cattle had perforated corneas. He arranged for serum vitamin A to be done and a number of patients with affected eyes had low levels. The worst case was a little girl who lived only 10 miles from the hospital. Her mother had a flock of sheep, but she was fed only oatmeal. Both corneae were perforated more than once, even while receiving vitamin A injection when her blood vitamin A was noted to fall rapidly.

Is there anyone out there who knows of the present position among the Navajo and people like them? There are many places now experiencing unprecedented drought, and as the case of the little girl shows yet again, xerophthalmia is often a disease of 'poverty in the midst of plenty'. Finally, I seriously question the efficacy of the injected vitamin A in this case. It has been known for years and publicised in WHO and IVACG documents that oily vitamin A when injected stays in the muscle and is not taken up into the circulation. Only water-miscible preparations are utilized by this route. Normally therapy and prophylaxis should be oral.

SURVEY IN MALI

Karin Kortlang and Jeanine Koster, students of the Royal Tropical Institute, Amsterdam under supervision and with assistance from a Malinese ophthalmologist carried out a study of the prevalence of blindness and impaired vision in Segou region in the summer of 1990. A study of xerophthalmia was included. Local terms for night-blindness occurred, namely 'souranfie' in Bambara and 'pike' in Peul. The impression was gained that available vegetables are not fed to young children.

5871 people were examined, 1172 children under 5 years. Among the latter XN was 3.16% and X1B 2.30%. EPI coverage seemed to be inversely related to xerophthalmia and it was suspected that many cases might be related to measles. Between the two population groups, Bambara and Peul, there was no significant difference in xerophthalmia rates in under 5s (3.9% and 2.2% resp). Although the Peul live on cattle breeding they are nomads and might suffer from food shortages first.

XEROPHTHALMIA IN EAST JAVA: 1975-77 and 1990

The same team carried out the surveys on both occasions. Full details of methodologies and findings are given in a limited circulation report prepared by Dr Kardjati and Professors Radjamin and Kusin. Eye signs in 1975-7 were X1A-B (highest 3.4%); and X2-3 (highest 0.2%) and XS (highest 0.2%). In 1990 among 2,892 boys and 2,921 girls under 5 years there was no XN, only 1 boy with X1B and no corneal lesions. The authors conclude that xerophthalmia has ceased to be a public health problem in East Java. It was considered that overall improvement in nutritional status was most likely responsible for this. It is recommended that the consumption of dglv be

increased but that it would be premature to terminate the distribution of vitamin A capsules. The coverage of these should be improved.

XEROPHTHALMIA IN UGANDA

Dr Medi Kawuma, Head of the Department of Ophthalmology at Makerere has produced a preliminary report on a vitamin A deficiency prevalence survey carried out in Kamuli District from October – December 1991. 59 villages randomly selected yielded a study population of 5074 children aged under 6 years. WHO criteria for a public health problem were exceeded (XN-2.7%, X1B-1.0%; X2-0.2%; X3A,B-0.1%; and XS-1.7%). Preliminary analysis showed an association between xerophthalmia and delayed milestones, wasting, lack of breast feeding, and infections. (Ed. Although this does appear to reveal a problem in Kamuli it should be pointed out to readers that a study confined to three months of one season of the year should not be considered to provide evidence representative of the prevailing situation).

BOOK REVIEW

WHERE THERE IS NO DOCTOR; A VILLAGE HEALTH CARE HANDBOOK – David Werner with Carol Thuman and Jane Maxwell. Revised English edition May 1992. Hesperian Foundation, California

$13.00 (+ $1.00 overseas shipping) **special price developing countries $6.00** from The Hesperian Foundation; P.O. Box 1692, Palo Alto, CA 94302, USA. fax (415) 325-9044.

Over about a quarter of a century 2 million copies have been printed in over 50 languages – surely a good second or third to the Bible!

Every effort is made to make it possible for the expected reader – the village health worker in a developing country – to be able to use fully what is written and illustrated. The language is as simple as possible, the diagrams are clear and telling (all by David Werner), the material is well ordered, indexed and grouped in sections with different page colours for ready reference. The paper is of noticeably better quality than some previous printings; an important point in the tropics.

Those familiar with the previous edition will want to know what is new. A section of about 20 pages is entirely new – dealing with such topics as AIDS, complications from illegal abortions, pesticide poisoning, drugs addiction and measuring blood pressure. Within the main text there is revised material on some aspects of diet, ORS, sterilizing equipment, VIP latrine etc. With about 450 pages to scan there are probably also many smaller improvements. The author has always asked for suggestions and rightly points out that local circumstances will often make a difference to details, although principles remain the same.

I would like to see more on the important topic of 'hot and cold' foods; special health problems in the rapidly growing slums of the third world, coping with lactation failure, and contraceptive effect of total breast feeding. Other points are inclusion of something on emergency treatment of a heart attack, herpes ophthalmicus, salt and hypertension, toxicity of some herbal teas, and preparation of cassava, which is often the staple food, to avoid toxicity.

It is twice stated that one third of all polio cases up to 2 million per year according to some, result from injections. I cannot find reference to this in standard texts but the care they advise is certainly correct. The sections on vitamin A and xerophthalmia have been revised and expanded and are excellent. I make two suggestions – large vitamin supplements should not be given during lactation as the mother may have recently conceived; and vitamin A is best given orally unless there is persistent vomiting; oily injection is not utilized.

None of these minor criticisms in any way detracts from the overall excellence of the book. I wonder how many doctors or clinical officers know anywhere near as much as what is contained here or, sadly, have regular access to even some of the medicines described. Perhaps the launch of the new edition would be a good time to have its actual use and its value as a health care tool evaluated. Would USAID or someone else take it on?

Donald S McLaren

NOTES AND NEWS

BELLAGIO BRIEF – on Vitamin A Deficiency & Childhood Mortality. An account of the conference held in Bellagio, February 3-7, 1992 was reproduced in our July issue. Copies of the conclusions of the meeting, together with a scientific rationale, list of participants and a reference list is now available from Helen Keller International (15 West 16th Street, New York, NY 10011, USA). Later this year they will also have this document available in French and Spanish as well as the complete proceedings of the meeting.

WORLD HEALTH ORGANIZATION documents A45/17 and WHA45.33 entitled "National Strategies for Overcoming Micronutrient Malnutrition" and Report of a Joint WHO/USAID/NEI Consultation of Principal Investigators on "Vitamin A Mortality and Morbidity Studies" are available from Nutrition Unit, WHO, CH-1211 Geneva 27, Switzerland. The following extract may be of special interest "At least 40 million preschool children are vitamin A deficient, of whom 13 million already have some eye damage (about 10m in SE Asia, 1.4m W. Pacific, 1.3m Africa, 1.0m E. Mediterranean, and 0.1m Americas). Every year between 250,000 and 500,000 preschool children go blind, partially or totally, from vitamin A deficiency. It is estimated that almost two thirds of these children die within a few months of going blind. The number of preschool children actually at risk of vitamin A deficiency and its consequences (blindness, increased mortality, decreased immunity) is estimated to be around 190 million. However, school-age children have also been shown to suffer from vitamin A deficiency xerophthalmia in some areas of the world. Women of child-bearing age in populations where xerophthalmia occurs could also be considered at

risk in view of the possibility of their producing infants who are vitamin A deficient at birth. The inclusion of both these groups swells the global estimates of those at risk to about 800 million. The majority of vitamin A deficient populations are in 37 countries, half of which are in Africa. However, because of the larger populations in affected Asian countries, two thirds of vitamin A deficient children are found in South-East Asia".

MOTHERS AND CHILDREN – Vol 11, No. 1 (Clearinghouse, American Public Health Association, 1015 15th Street NW, Washington DC 20005, USA). This issue includes an item on Participatory Action for vitamin A by Suttilak Smitasiri from N.E. Thailand.

DIALOGUE ON DIARRHOEA – issues no. 48 (decisions about diarrhoea; traditional healers; viral diarrhoeas; persistent diarrhoea) **no. 49** (exclusive breast-feeding; diarrhoea and low birth weight; cholera guidelines; low cost sewerage), (AHRTAG, 1 London Bridge Street, London SE1 9SG, UK).

DIARRHOEAL DISEASE CONTROL PROGRAMME, WHO – Eighth Control Programme Report 1990-91 and Report of 13th Technical Advisory Group from DDCP, WHO, CH-1211 Geneva 27, Switzerland. The World Summit for Children in 1990 specified that child mortality due to diarrhoea should be reduced by 50% between 1990 and 2000. Globally, significant proportions of diarrhoeal deaths are now caused by persistent diarrhoea (35%) and dysentery (15%). Four new key indicators for measuring programme progress have been defined: the use of ORT and continued feeding for diarrhoea cases; access of the population to ORS; case management in health facilities; and mothers' knowledge of home case management. A meta-analysis of 13 trials of rice-based ORS concluded it produced a significant reduction in stool output in the first 24 hours in patients of all ages with cholera, but the effect on non-cholera diarrhoea in children was much smaller. Other studies concluded that the inclusion of maltodextrin or various amino acids in ORS formulation produced no practical benefit in treating acute watery diarrhoea in children.

Also from the DDCP is a monograph "The potential of traditional technologies for increasing the energy density of weaning foods: a critical review of existing knowledge with particular reference to malting and fermentation" by A Ashworth and A Draper. "The current interest in traditional food-processing technologies, as they relate to weaning foods, lies in their potential for (i) reducing pathogen contamination, and (ii) increasing energy density. The paper examines the latter and focuses on malting and fermentation. Malting has the potential to increase energy density of weaning foods, but its effectiveness in improving the energy intakes of young children has not yet been demonstrated. The costs involved in terms of time, labour and space, and negative attitudes which associate malting with alcohol, may constrain its feasibility. Fermentation is unlikely to have any substantial effect on the energy density of weaning foods, but it does have other important benefits".

ARAVIND HOSPITALS, ACTIVITY REPORT 1991. Among the many clinical, teaching, research and field activities reported vitamin A deficiency continues to receive attention. An exhibition on the role of vitamin A in the prevention of nutritional blindness was mounted on March 22 and from April 3-5 a workshop on vitamin A deficiency and its control for participants from all over India was held (1 Anna Nagar, Madurai – 625 020 Tamilnadu, India).

VITAMIN A NEWS NOTES, Spring 1992 issue No. 8 (HKI, 15 West 16th Street, New York, NY 10011, USA). A biannual publication available in English, French and Spanish; funded by AID. This issue features various private and voluntary organisations' activities around the world – Kiribati, Haiti, Senegal, Mauritania, Nepal, and Bangladesh; steps towards eliminating vitamin A deficiency by the year 2000 (article by A Sommer) and local terms for nightblindness in selected countries.

CONTACT, No. 124, April 1992 bimonthly from Christian Medical Commission, World Council of Churches, 150 route de Ferney, 1211 Geneva 2, Switzerland. Topic – **"Health Development Among the Nomadic Peoples of East Africa"**. Accounts of programmes among the Maasai and other nomadic groups "illustrate cases of peaceful coexistence between traditional and western approaches".

HEALTH HERALD – Agency for International Development, Office of Health Newsletter No. 6, July 1992.

NESTLE FOUNDATION ANNUAL REPORT 1991 – (4, Place de la Gare, CH-1003 Lausanne, Switzerland). Includes activities in 1991 and review articles on 'the new British dietary reference values', 'the RQ/FQ concept and body weight maintenance', 'whole-body protein turn-over and resting energy expenditure in pregnant Gambian women'.

NUTRITION NEWS, Vol. 13, No.'s 1,2, 1992 (National Institute of Nutrition, Tarnaka, Hyderabad, 500 007, India). Reviews are on 'respiratory infection and riboflavin status' and fish for a healthy heart'. The Annual Report for 1990-91 has recently been published. "The Institute continued its efforts to find simple and feasible solutions to the existing nutritional problems, through community studies and operational research. While efforts are being made to develop alternative strategies like horticultural intervention to improve vitamin A status, action was taken simultaneously to operationalise the available technology like iron fortification of salt for the control of anaemia. Equal importance was given to clinical and basic research. Clinical studies were focused on maternal and child nutrition, energy metabolism and diet related diseases like diabetes, hypertension and cancer. Basic research included studies on folic acid catabolism, role of ferritin, and biochemical basis of brunescent cataract. Highlights of research contributions in other areas are included".

IAPB NEWS, No. 16, June 1992 – Newsletter of the International Agency for the Prevention of Blindness, from P.O. Box 191, Haywards Heath, West Sussex RH16 4YF, UK. This issue includes an article on vitamin A deficiency.

SIGHT & LIFE, Vol 7, No. 1, July 1992 (F. Hoffmann-La Roche Ltd, P.O. Box CH-4002 Basle, Switzerland). This issue has three features: (i) a lecture given at Hoffmann-La Roche headquarters by Dr Felix Ezepue, a young Nigerian ophthalmologist from Enugu where he is a lecturer in the medical school and teaching hospital. He had successfully completed the Diploma Course in Community Eye Health at the Institute of Ophthalmology, London, supported by Sight & Life. His topic was 'Vitamin A deficiency and childhood blindness in Enugu, Nigeria, (ii) a curriculum vitae of Dr J.C. Bauernfiend who worked at Nutley for many years on vitamin A and carotene; and iii) a vitamin A poster (in English – from Task Force Sight and Life, P.O. Box 2116, 4002 Basle).

THE VITAMIN A+ SIEVE; issue 92-2, July 1992 (published semiannually by Rodale Press Information Services, 33 E. Minor St., Emmaus, PA 18098, USA). Includes abstracts of papers (with addresses), comments on issues, accounts of programmes and news.

NEWS ON HEALTH IN DEVELOPING COUNTRIES, Vol. No. 5, December 1991. Published three times a year, free of charge (International Child Health Unit, entrance 11, S-751 85 Uppsala, Sweden). Each issue is devoted to a theme, this on Breast-feeding Promotion. The next issue is on Vitamin A.

AHRTAG Primary Health Care Courses – Directory for 1992/3 now available (free in developing countries from 1 London Bridge Street, London SE1 9SG, UK). Also available revised edition of "How to look after a refrigerator" (Price £5 plus postage and packing, order from TALC, P.O. Box 49, St Albans, Herts AL1 4AX, UK).

NUTRITION CENTER OF THE PHILIPPINES has produced a calendar for 1992 which is designed as a counselling tool to be used by nurses and midwives. It carries key health and nutrition messages which mothers should know and practise. From Nutrition Center of the Philippines. MC P.O.Box 653, Makati, Metro Manila, Philippines.

HUMAN NUTRITION INSTITUTE OF INTERNATIONAL LIFE SCIENCES INSTITUTE in November 1991 joined with US Centers for Disease Control and the Program Against Micronutrient Malnutrition to hold a technical workshop on "Coordinated Strategies for Controlling Micronutrient Malnutrition". The report of this meeting is available from Suzanne S. Harris, Executive Director, Human Nutrition Institute, 1126 Sixteenth St, N.W., Washington, DC 20036, USA. At the same address are available reports of two Conferences of the International Nutrition Planners Forum (INPF) entitled Effective Nutrition Communication for Behavior Change, and Crucial Elements of Successful Community Nutrition Programs.

THE STATE OF WORLD POPULATION 1992 – United Nations Population Fund, 220 East 42nd Street, New York, NY 10017, USA. This report lays its main emphasis on what it calls Sustainable Development defined as 'development that meets the needs of the present without compromising the ability of future generations to meet their own needs'; it means 'improving the quality of human life while living within the carrying capacity of supporting ecosystems'.

In mid-1992 world population was 5.48 billion. Annual additions in the next decade will average 97 million, the highest in history, nearly all this growth will be in Africa, Asia and Latin America. Some 83 per cent of growth in this time will be in urban areas. 2.39 billion people are urban dwellers, 63 per cent of these are in developing countries.

In countries where population growth slowed in the 1980's the following benefits were seen: average incomes per person grew 2.5 per cent a year faster than those with more rapid growth; savings and investment ratios were higher.

LITERATURE DIGEST

Vitamin supplementation and child survival. Lancet 1992: 340:267-71. Herrera MG et al, Harvard Institute for International Development, 1 Eliot Street, Cambridge MA 02138, USA. In a double-blind, placebo-controlled trial of vitamin A supplementation in the Sudan among 28, 753 children aged 9-72 months at risk of vitamin A deficiency children were assigned to receive either 200,000IU vitamin A and 40IU vitamin E every 6 months (vitamin A group) or 40IU vitamin E (placebo group). During the 18 months of follow up there were 120 deaths (8.4/1000) in the vitamin A group and 112(7.9/1000) in the placebo group (relative risk 1.06, 95% confidence interval 0.82-1.37). Controlling for geographic site, round of observation, anthropometry, morbidity, dietary intake of vitamin A, sex, and all baseline differences between the two groups did not change the results. Children living in poor and unsanitary environments, younger children, and those sick, stunted, wasted, or consuming diets low in vitamin A were at significantly higher risk of dying.

Vitamin A deficiency and attributable mortality among under-5-year-olds. Bull Wld Hlth Org 1992; 70:225-32. Humphrey JH et al, Johns Hopkins University, 120 Wilmer, 600 North Wolfe Street, Baltimore MD 21205-2179, USA. Reported are estimates of the prevalence in developing countries of physiologically significant vitamin A deficiency and the number of attributable deaths. The WHO classification of countries by the severity and extent of xerophthalmia was used to categorize developing countries by likely risk of subclinical vitamin A deficiency. Using vital statistics compiled by UNICEF, population figures and mortality rates for under-5-year-olds were derived. The findings of vitamin A supplementation trials were applied to populations at-risk of endemic vitamin A deficiency to estimate the potential impact of vitamin A nutriture in reducing mortality during pre-school years. Worldwide, over 124 million children are estimated to be vitamin A deficient. Improved vitamin A nutriture would be expected to prevent approximately 1-2 million deaths annually among children aged 1-4 years. An additional 0.25-0.5 million deaths may be averted if improved vitamin A nutriture can be achieved during the latter half of infancy. Improved

vitamin A nutriture alone could prevent 1.3-2.5 million of the nearly 8 million late infancy and pre-school age child deaths that occur each year in the highest-risk developing countries.

Micronutrient deficiencies in refugees. Lancet 1992;339: 1214-5. Toole MJ, Centers for Disease Control, Atlanta, Georgia, USA. This is a report of a one-day technological review. (Ed. Most attention focussed on vitamins A, C, niacin, thiamin and iron. For xerophthalmia only one report was cited, Eastern Sudan in 1985. The problem is much more widespread and not all aid agencies are informed. A severe outbreak was reported very recently from Ethiopia, aid food was devoid of vitamin A. As a poignant follow-up to this Tomkins and Henry (Lancet 340:367-8) made a comparison of a typical refugee ration for a day – 400-500 g cereal (wheat, rice, corn), 30g lentils/legumes, 20g oil and about 5g sugar – with a pet food. Four vitamins and iron were quite inadequate in the ration, but it was completely devoid of vitamin A. The pet food had an excellent micronutrient composition by contrast. This provides a sorry indictment of North-South attitudes and priorities).

Conjunctival impression cytology with transfer as a field-applicable indicator of vitamin A status for mass screening. Int J Epidemiol 1992; 21:373-80. Carlier C et al, U 56 INSERM, Unite de Recherche en Hepatologie Pediatrique, Hopital de Bicetre, le Kremlin-Bicetre, France). A formula is proposed for developing a prevalence criterion for estimating the prevalence of subclinical vitamin A deficiency as assessed by this technique. This would be comparable to the criteria proposed by WHO, and used universally now, for detecting the occurrence of a xerophthalmia problem of public health magnitude.

Influence of enteral parasites on the blood vitamin A levels in pre-school children orally supplemented with retinol and/zinc. Europ J Clin Nutr 1991; 45:539-44. Marinho HA et al, Instituto Nacional de Pesquisas da Amazonia, Cx. Postal 478, Manaus, Amazonas, 69011, Brasil. 240 children with ascaris and/or **Giardia lambia** infestation were divided into two groups. One was treated with anthelminthic. All were given daily either 5 mg zinc acetate, 500 ug retinol acetate or placebo for 30 days. Retinol and/or zinc raised blood levels of vitamin A only in children who were parasite-free. Supplements made little difference to vitamin A levels in children not treated first for the parasites.

Vitamin A supplementation enhances specific IgG antibody levels and total lymphocyte numbers while improving morbidity in measles. Pediatric Infect Dis J 1992; 11:203-9. Coutsoudis A, Dept Paediatrics and Child Health, P.O. Box 17039, Congella 4013, Republic of South Africa. Supplementation was associated with higher lymphocyte counts and higher mean measles IgG antibody levels and fewer respiratory symptoms after recovery.

Breast feeding in the first six months: no need for extra fluids. Brit Med J 1992; 304:1068-9. Martines JC et al, Diarrhoeal Disease Control Programme, WHO, 1211 Geneva 27 Switzerland. In developing countries most mothers supplement breast milk with water or teas. It is commonly believed that this is necessary to quench thirst, relieve colic, earache etc.

Studies in Brasil, Philippines and Peru have shown that this practice predisposes to diarrhoea and the intake of milk is reduced in comparison with exclusive breast feeding. Six studies undertaken to measure the urine osmolality of healthy, exclusively breast fed infants showed conclusively that even in dry and hot environments they received adequate water and electrolyte intake. This message should be put across by health practitioners and the rights of working women to continue to breast feed protected. An information sheet has been produced by WHO on this topic, entitled "Facts about infant feeding" – available from CDR Division, WHO, 1211 Geneva 27 Switzerland.

Liver fibrosis: better understanding may help diagnosis and treatment. Brit Med J 1992; 305:537-8. Burt AD, School of Pathological Sciences, University of Newcastle upon Tyne, Newcastle NE 1 4LP, UK. Recent studies have shown that the matrix proteins responsible for this process originate mainly in the perisinusoidal cells (fat storing, lipocytes, Ito, stellate cells) which are normally replete with vitamin A in the form of retinyl ester. Liver injury results in hypertrophy of the endoplasmic reticulum and loss of retinyl esters.

A method for determining concentrations of retinol, tocopherol, and five carotenoids in human plasma and tissue samples. Amer J Clin Nutr 1992; 56: 417-26. Nierenberg DW, Nann SL, Depts of Medicine and Pharmacology, Dartmouth Medical School, Hinman Box 7506, Borwell Building 630E, Lebanon, NH 03756, USA. The greatest advantage of this method is that enzymatic digestion enables tougher tissues to be made susceptible to mechanical homogenisation without encountering some of the problems associated with saponification.

Metabolism of carotenoid analogs in humans. Amer J Clin Nutr 1992; 56:433-9. Zeng S, Furr HC, Olson JA, Dept of Biochemistry and Biophysics, Iowa State University, Ames, Iowa 500011, USA. The metabolism of three analogs used was very different. Kinetically, the maximum serum concentrations, areas under the curve, and mean sojourn times for the three analogs differed by 50-, 270-, and 5-fold respectively.

Plasma carotenoid response to chronic intake of selected foods and B-carotene supplements in men. Amer J Clin Nutr 1992; 55:1120-5. Micozzi M et al (reprint requests PR Taylor, Cancer Prevention Studies Branch, National Cancer Institute, Executive Plaza North, Suite 211, Bethesda, MD 20892, USA). In 30 men serial plasma changes in alpha-carotene, beta-carotene, lutein/zeaxanthin, and lycopene were studied. Compared with baseline, beta-carotene increased in capsule and carrot groups, alpha-carotene increased in the carrot group and lutein increased in the broccoli group. Lower lutein in recipients of beta-carotene capsules suggested and interaction between these two carotenoids. Lycopene declined in all groups except the tomato-juice group.

Xerophthalmia and growth in pre-school Indonesian children. Amer J Clin Nutr 1992; 55:1142-6. Tarwotjo I et al (reprint requests to J Katz, Dana Center for Preventive Ophthalmology, Room 120 Wilmer, The Johns Hopkins University, 600 N Wolfe Street, Baltimore, MD 21205, USA). About 4000 children were examined for xerophthalmia and weighed and measured at 3-mo intervals. Children recovering from xerophthalmia over 3-mo gained 124 g on average more than normal children. Those who developed xerophthalmia over this period gained 199g less and grew 0.28 cm less than normal children. Children with chronic xerophthalmia gained 120 g less and grew 0.21 cm less than normal. Poor linear and ponderal growth patterns were independent of the presence of diarrhoea or respiratory infections.

Nutrient intake and cataract extraction in women: a prospective study. Hankinson SE et al. Brit Med J 1992; 305:335-9. Channing Laboratory, 180 Longwood Avenue, Boston, MA 02115, USA. Dietary intakes of vitamins A, C and E, carotene and riboflavin were measured in 50828 female registered nurses aged 45-67 years. 493 cataracts were extracted over the follow-up period. Intake of carotene and vitamin A was inversely related to cataract. Vitamins C, E and riboflavin were not related. Spinach, rather than carrots, the greatest source of beta-carotene, was most consistently associated with a low relative risk.

Retinyl palmitate hydrolase activity in human liver. Mourey M-S, Amedee-Manesme O. Amer J Clin Nutr 1992; 55:729-33. INSERM Unite 56, Hopital de Bicetre, 78 rue de General Leclerc, 94270 le Kremlin-Bicetre, France. Enzymatic activity was found to be very variable and no clear relationship with vitamin A status could be found.

Effects of timing and dose of vitamin A on tissue retinol concentrations and antibody production in the previously vitamin A-depleted rat. Amer J Clin Nutr 1992; 55:443-51. Pasatiempo AMG et al (reprint requests to AC Ross, Department of Physiology/Biochemistry, Medical College of Pennsylvania, 3300 Henry Avenue, Philadelphia PA 19129, USA). Various vitamin A-repletion protocols successfully restored the tissue retinol concentrations of vitamin A-depleted rats within a few hours to a day after dosing. However, not all doses of retinol that caused tissue storage were effective in restoring antibody response within the time studied. The most effective protocol was the divided dose given so that repletion began a few days before challenge with pneumococcal poylsaccharide.

Plasma B-carotene response in humans after meals supplemented with dietary pectin. Amer J Clin Nutr 1992; 55:96-9. Roack CL, Swendseid ME, Program in Human Nutrition, School of Public Health, M5541 SPHII, The University of Michigan, Ann Arbor, MI 48109-2029, USA. When pectin was added to a meal the mean per cent increase in plasma B-carotene concentration was reduced by more than a half. This inhibitory effect of pectin may provide one explanation for observation of reduced plasma B-carotene response after ingestion of carotenoid-rich foods as compared with equivalent doses of B-carotene supplements.

Socio-economic correlates of child nightblindness in a coastal area of Bangladesh: a critical analysis. Ecol Food Nutr 1992; 28:149-56. Islam MN, Yusuf HKM (reprint requests to HKM Yusuf, Dept of Biochemistry, University of Dhaka, Dhaka-1000, Bangladesh).

In three villages in Bhola District 1642 children under 6 years were examined. 68 were nightblind. The prevalence in girls was 4.4% and 3.9% in boys (Ed. the sex ratio is usually reversed, but the difference was not significant: p=0.74). While the level of formal education was not related, nutritional knowledge of the head of the family was, as was intake of vegetables and oil. There was less nightblindness in fisher families and this was attributable to habitual inclusion of fish liver in the family diet, and not to level of nutritional knowledge. Poverty and illiteracy in this community were not in themselves responsible. 67.4% of the non-nightblind families were totally illiterate, and only 50.0% of the nightblind group. Many of the former had been exposed to the constant delivery of nutritional messages on radio and television. (Ed. more studies of this kind are needed in very different ecological circumstances and with different levels of exposure to preventive measures. They will help to monitor the effectiveness of programmes and suggest where attention in the future may profitably be directed).

Potential role of beta-carotene in the prevention of cardiovascular disease. Int J Vit Nutr Res 1991; 61:277-91. Gerster H, F Hoffmann La Roche, Grenzacherstrasse 124, 4002 Basel, Switzerland. It has recently been hypothesised that LDL (low density lipoproteins) only become atherogenic if they have been oxidised within the arterial wall. Naturally occurring antioxidants such as vitamins C and E, and beta-carotene would be preferable preventive agents to drugs. The oxidation of PUFAs in LDL involves the generation of singlet oxygen, of which beta-carotene is a powerful quencher. Most of the older epidemiological studies have not included beta-carotene and other carotenoids. In the United States the Physicians' Health Study indicates that patients with stable angina pectoris who took 50mg beta-carotene every other day for more than 2 years experienced only half as many cardiovascular accidents as those taking placebo. The study continues to determine whether beta-carotene also has a primary prevention role.

Cis-trans Isomers of lycopene and B-carotene in human serum and tissues. Stahl W et al. Arch Biochem Biopny 1992; 294:173-7 (reprint requests H Sies, Institute fur Physiologische Chemie I, Universitat Dusseldorf Moorenstr 5,4000 Dusseldorf, Germany). In addition to all trans-lycopene, at least 3 cisisomers were present, accounting for more than 50% of total lycopene. 13- and 15-cis-B-carotene were present at only 5% of the all-trans isomer. 9-cis-B-carotene was present in tissue samples but not in serum. Liver, adrenal and testis always contained significantly higher concentrations of carotenoids than kidney, ovary or fat. B-carotene was the major carotenoid in liver, adrenal, kidney, ovary and fat. Lycopene predominated in testis.

Alterations in cytokeratin expression precede histological changes in epithelia of vitamin A-deficient rats. Cell Tissue Res 1992; 268:197-203. Gijbels MJJ et al, TNO Institute of Ageing and Vascular Research IVVO, P.O. Box 430, NL-2300 AK Leiden, The Netherlands. No change in cytokeratin expression was seen in trachea, skin, liver and colon. It did occur in urinary bladder and salivary glands and was concomitant with a substitution of cytokeratins 4, 5+8, 7, 18 and 19 by cytokeratin 10. The latter is specific for keratinized squamous epithelium. Cytokeratin expression changed in bladder, ureter, kidney, salivary glands, uterus and conjunctiva before histological alterations appeared. (Ed. we should expect this technique to be applied to conjunctival impressions in the near future. It should help in overcoming some of the difficulties experienced with CIC (see editorial in Lancet 1992; 339:1514-5).

Effect of food preparation on qualitative and quantitative distribution of major carotenoid constituents of tomatoes and several green vegetables. J Agric Food Chem 1992; 40: 390-8. Khachik F et al, Nutrient Composition Laboratory, Beltsville Human Nutrition Research Center, Building 161, BARC-East, Beltsville, MD 20705, USA. The predominant carotenoids in raw green vegetables were neoxanthin, violaxanthin, lutein epoxide, lutein, alpha-carotene and beta-carotene. The effect of various means of cooking were extensively studied. While epoxycarotenoids were somewhat sensitive to heat treatment, lutein and hydrocarbon carotenoids such as alpha-and beta-carotene, lycopene, neurosporene, gamma-carotene, phytofluene, and phytoene survived heat treatments.

Epidemiology of childhood blindness. Eye 1992; 6:173-6. Foster A, Gilbert C, ICEH, Institute of Ophthalmology, Bath Street, London EC1V 9EL. Of the estimated 1.5 million blind children in the world 1.3 m live in Asia and Africa and probably 75% of causes are preventable or curable. More information is needed on the magnitude and severity of visual loss in children in different parts of the world, and on the changing patterns of childhood blindness over time in individual countries. This information, when available for each country, should be used to develop a co-ordinated and integrated control programme against the important causes of avoidable blindness in children in each individual country.

XEROPHTHALMIA BULLETIN

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Supported by Sight Savers (Royal Commonwealth Society for the Blind) and the International Vitamin A Consultative Group

Bulletins are *sent free* to anyone seriously concerned with xerophthalmia
Please apply for membership to the Editor

THAT SPINACH AGAIN!

In an editorial reviewing a paper on the variability of young children's energy intake Dr. Gilbert Forbes (New Eng J Med 1991; 324:262-3) wrote "Eat, eat, clean your plate". And on other occasions, "Don't eat all those cookies; you'll spoil your supper". How many times have those words issued from the mouths of parents whose young children seem — as my own did years ago — not to be eating properly? Many can recall the New Yorker cartoon showing a defiant child at the dinner table: "I say it's spinach, and I say the hell with it!" Perhaps the artist had read Clara Davis' classic paper (Am J Dis Child 1928; 36:651-79) on the success of self-selected diets for young children, for of the many foods offered to her subjects spinach was almost always refused. Could this aversion possibly result from the high oxalate and nitrate content of this vegetable?"

THOUGHTS OF A CHILD BLIND DUE TO MALNUTRITION

They say that two eyes mean all the richness...
but I do not have them now.
When you look at me, you cry sadly.
If you only knew that it was because of you,
my mother and grandmother.

You loved me, but you did not know how to feed me, or how to care for me,
when I was sick.

When I got measles, you put me in a dark room,
where I could not see any daylight,
and you never cleaned me with water.

When I got diarrhoea, you stopped giving me your breastmilk, mother,
and you grandmother,
forbade giving me fish and shrimps.

You sold vegetables, bananas, oranges and eggs and bought sodium glutamate to add to my rice soup, with which you fed me.

By doing so, you were comforted, while I was hurt. Because of this, my eyes are covered by darkness now.
It will last all my life, though you are crying sadly, days and nights.

This touching poem was composed by a Vietnamese health worker and was presented at group work exercises during a seminar in Hanoi some years ago. It is reproduced from the Vitamin A issue of "News on Health in Developing Countries" reviewed in this bulletin.

200,000 IU VITAMIN A CAPSULES

Professor John Hansen has written from Johannesburg to say that he was recently informed by the local vitamin A distributor that head office had withdrawn these capsules. He says that the vitamin 'now has to be given by breaking open capsules which is much more expensive and awkward. Have others had the same problem?' We shall be requesting clarification from the company and in the meantime we should be grateful to hear from others in the field who have had the same experience

2

AN APPROACH FOR PREVENTION OF NUTRITIONAL BLINDNESS IN CHILDREN

by
Dr. Gopa Kothari
Adviser — Child Development Services
Sight Savers, India

Of the many problems which confront the children of the world today, the problem of malnutrition is probably the foremost. While there are reasonable prospects of our being able to control some of the major communicable diseases in the next two to three decades, all current indications with respect to population growth and economic trends point to serious aggravation of the problem of malnutrition by the year 2000 A.D. The challenge posed by malnutrition, formidable as it is at present, threatens to assume even more serious dimensions in the coming decades.

Malnutrition in its various forms is a very depressing health problem of today. Some facts are known to all of us. More than 200 million young children wait today to be released from hunger. An estimated 10 million of them are at any given moment, in the grip of severe protein energy malnutrition. Ten millions of the world's children are vitamin A deficient; one million or more needlessly die or go blind every year.

It is also known that vitamin A deficiency increases mortality, especially, among children of 6 months to 6 years and also increases severity, complications and risk of death from measles and increases childhood morbidity particularly the severity of infection episodes like diarrhoea and pneumonia.

The widespread malnutrition prevalent among the poor socioeconomic groups of developing countries is attributed to economic factors. While poverty is an important limiting factor for buying enough food, the rampant malnutrition and vitamin A deficiency is not all due to poverty. There is a widespread ignorance about child care including nutritional requirements and the common foods that supply the necessary nutrients. Faulty feeding habits arising from ignorance, superstitions and wrong beliefs must be considered as being responsible factors for aggravating malnutrition and vitamin A deficiency in children.

The problem of xerophthalmia has always received importance as a specific condition of ill health as the surface symptom, but very little is done to tackle the underlying cause. So long as we continue to treat the symptom without really getting down to identification and elimination of the underlying primary causes, we are unlikely to make much impact. If we continue our approaches based upon 'Symptomatic Medicine' (vitamin A prophylaxis programme) without incorporating the practical measures to deal with root causes, the toll of vitamin A deficiency, deaths and blindness amongst the

are many constraints which make the task of dealing with primary causes seem to be impossible, but nevertheless, we must work within the realities of the existing situation, keeping in mind the real needs of the community and develop an appropriate programme.

Knowledge acquired in the past few decades, has provided us clarification on human nutrition education, not only formal education but non-formal education, adult education and extension activities in the community. This knowledge has strengthened the scientific justification for nutrition education that it should not be divorced from educational motivation towards altering living patterns to increase the physical fitness and caloric expenditure for the individual within the reach of society.

To control nutritional blindness among children, the principal target at the family level for nutrition education is the mother. She needs to be educated on the selection of the right kinds of local foods which are rich in vitamin A and in the planning of a nutritionally adequate diet within the limits of her purchasing power.

The main objective of nutrition education to control vitamin A deficiency is to increase the consumption of vitamin A — containing foods per week by the pregnant and lactating mothers and the proportion of infants eating vitamin A-rich foods by the age of 12 months.

The approach needs more innovation, initiative and integration for implementation by emphasising on complementing existing diets and modifying dietary practices, that are feasible and not on imparting just mass general information. Harmful food taboos and dietary prejudices can be identified and corrected. The promotion of breast feeding and improvement in infant and child feeding practices are the two main areas where nutrition education can be focussed.

The problem of vitamin A deficiency encompasses the economic, social and cultural causes, and hence, it is necessary to make the nutrition education activities more practical and socially relevant and link these activities with activities like the formation of women's groups and improving the status of women through literacy, general awareness, health awareness and income generating activities. The development of such inter-sectoral co-ordinated programmes with the active participation of women will help to break the vicious cycle of illness, poverty, malnutrition, illiteracy and ignorance among women and children. It will gradually bring about the desired changes in the diet of pregnant and lactating mothers and in child feeding and rearing practices, ultimately resulting in improvement in child nutrition and prevention of nutritional blindness.

No blue print can be provided for the control of xerophthalmia, but certainly it needs a

flexibility to accommodate and facilitate modifications suited to the needs of the local community.

The development of such a programme will also demand reorientation of doctors, social workers, nutritionists, other professionals and para professionals working in the field. It is essential to change the attitude of "hospital or ivory tower outlook" to "health and nutrition outlook" and "working in isolation" to "team approach".

Well-planned health and nutrition education activities with the community initiative especially the women groups, will lead to change in their habits and will culminate in better utilisation of existing health and nutrition programmes.

This will assure the development of programmes with steady steps towards better nutrition, better eye care, child survival and prevention of nutritional blindness in children and will bring us closer to the goal of Health for All by the year 2000 A.D.

PUBLICATIONS REVIEW

Nutrition Communications in Vitamin A Programs: A Resource Book, IVACG, 1992. Free to representives in developing countries and for US$3.50 to others. From IVACG Secretariat, The Nutrition Foundation Inc., 1126 Sixteenth Street N.W., Washington, D.C. 20036 USA.

This book uses many examples and full-color photographs in presenting experiences, facts, and visual and textual information to inspire creativity and action in those who combat vitamin A deficiency in the field. It will be a valuable resource for planning nutrition communication activities with large, ongoing vitamin A programs. The concepts and techniques presented are also relevant to other health and nutrition issues'.

French and Spanish Translations are now available of 'Combating Iron Deficiency Anemia Through Food Fortification Technology: An Action Plan', the latest publication of INACG (International Nutritional Anemia Consultative Group) and available as the above-mentioned IVACG publication.

Prevention of Childhood Blindness, WHO, Geneva, 1992. Price in developing countries Sw, fr. 10.50.

This short booklet (51 pages) is based on the presentations and discussions of participants at a workshop on childhood blindness which was held at the International Centre for Eye Health (ICEH) in London in May 1990.

The booklet is easy to read and does not assume detailed knowledge of childhood eye disease to be understandable and informative. The chapters are laid out logically, starting with available data on the magnitude and causes of childhood blindness, emphasising that in terms of "blind years" childhood blindness is a major public health problem, and that there is marked regional variation in aetiology. The following chapters describe the major blinding conditions, beginning with hereditary diseases and leading on to causes occurring during childhood. Conditions which are preventable and treatable are described in greater detail, as are the necessary control strategies. The final chapters describe how a multidisciplinary approach is required to control childhood blindness, and that collaboration is required between eye care programmes, health educationalists, nutritionists and non-governmental organisations and health ministries involved in the prevention of blindness.

Clare Gilbert, FRCS, FCOphth, Research Fellow, ICEH

Vitamin A Field Support Project (VITAL) (a project of the Aid Office of Nutrition, managed by the International Science and Technology Institute Inc. 1616 North Fort Myer Drive, Suite 1240, Arlington, VA 22209, USA)

A series of reports entitled Vitamin A Facts covers in three monographs comprehensive data from selected countries in Asia Region; Latin America & Caribbean Region; and Africa Region.

News on Health Care in Developing Countries. Special Issue: Vitamin A. Published four times a year, free of charge, by International Child Health Unit, Department of Pediatrics, Uppsala University, Sweden.

Each issue is devoted to a single topic and all of the articles in the 3rd number for 1992 relate to vitamin A. A team of international experts has been recruited to present authoritative accounts with the following titles — Hypovitaminosis A: Hidden Hunger? (BA Underwood); Detection of Vitamin A Deficiency Problem in a Community (DS McLaren); First Step for Child Survival: Preventing Vitamin A Deficiency among Women at risk (AL Ralte); Control of Vitamin A Deficiency in Africa (K Bailey); Development of a Vitamin A Control Programme-an Example from Tanzania (FP Kavishe); Combining Short-and Long Term Vitamin A Deficiency Control Programs (T Greiner); IVACG (A Horwitz, BA Underwood); Vitamin A Deficiency and Childhood Mortality (C Gopalan; A Sommer).

Child-to-Child: A Resource Book eds Grazyna Bonati and Hugh Hawes. The Child-to-Child Trust, London 1992. (£6.50 including postage and packing from TALC P.O. Box 49, St. Albans, Herts AL1 4AX, U.K.)

This book contains several separate booklets and other recent publications conveniently in one volume. Section 1 contains all the Child-to-Child Activity sheets and Section 2 "Approaches to Learning and Teaching" gives a detailed description of the C-to.C methodology with many examples. Section 3 offers practical advice on how to plan and organise an evaluation. There is also a list of publications.

(Ed. I am sure that devotees of this kind of approach will be glad to know this work is available and at such low cost. Without wanting

to seem critical, there does seem to be a welter of this kind of material, much of what is here is just like that in "Where there is no doctor". Part of the problem may be that health is such a boring subject; disease is unendingly fascinating! — just like good versus evil, peace versus war, poverty versus riches, age versus youth — quite a lot of evidence for original sin!).

Ending Malnutrition. Why Increasing Income is not Enough. Tonia Marek. World Bank Africa Technical Department. Technical Working Paper No. 5 October 1992 (World Bank, 1818 H Street, Room J4-147, Washington D.C. 20433, USA.)

This study suggests that increases in income of the poor cannot on its own be expected to raise food intake, but its effect on nutritional status may be enhanced by other measures such as more advantageous ways of paying people, offering nutrition education and providing women with functional literacy classes etc.

Folic Acid and the Prevention of Neural Tube Defects. Report of an Expert Advisory Group. Department of Health, UK 1992 (copies available from Health Publications Unit, Heywood Stores, No. 2 Site Manchester Road, Heywood, Lancashire, OL10 2PZ, UK). The main recommendation is that folic acid supplements at a daily dose of 5mgm should be advised for all those women who wish to become pregnant or who are at risk of becoming pregnant. Supplementation should continue until the 12th week of pregnancy.

Protein Energy Malnutrition. J.C. Waterlow, Edward Arnold, London 1992. Price £50.00.

This is the third book on this subject published by Arnold and in 400 pages brings it completely uptodate. It may come as a surprise to some readers to find that the aetiology of PEM is by no means a foregone conclusion and there are a number of issues that remain unresolved. This seems to be partly as a result of the relatively little clinical research currently underway. Space is found for only just over 20 pages on prevention, which is a sad commentary on the depressing outlook for the nutrition of the world's children as the year 2000 approches.

A Colour Atlas and Text of Diet-Related Disorders, 2nd edition, pp336, 561 plates most in colour, 114 Tables. By Donald S. McLaren. Published by Wolfe Medical Publications, London 1992. Price £49.50. A much enlarged and completely updated and revised edition of the most comprehensive book of its kind in this field.

LETTER FROM NIST

I would like to inform the readership that the National Institute of Standards and Technology (NIST) has been coordinating a quality assurance programme for fat-soluble vitamin and carotenoid measurements in serum for over 100 laboratories internationally have participated and measurement variability among participating laboratories has improved to less than 10% RSD for vitamin A. Three times during each year we send out 3 to 5 samples to laboratories participating in the quality assurance programme. They perform the analysis of vitamins and carotenoids and report the values to NIST. The samples are also measured at NIST using at least two methods. The data are tabulated and supplied to the laboratories in a form that permits them to see how their measurements compare to the grand mean and the NIST values. Laboratories are given a number so others can't associate the data with a laboratory (confidentiality). We also provide consultation to help laboratories identify possible sources of error in the methodology. In 1992 we instituted a "small" fee to offset the cost of sample handling and shipping so that the programme could be opened to all laboratories. The fee is $300/yr for the United States laboratories and $600/yr for those outside the USA. In 1993 we will begin to include food materials into the programme. NIST also has Standard Reference Materials (SRMs) for vitamins and carotenoids with certified concentrations assigned that are to be used for method validation and during the assignment of values to in-house control materials. For information regarding SRMs or participation in the NIST Fat-Soluble Vitamin Quality Assurance Programme contact:

Dr. Neal E. Craft
NIST
Building 222, Room B 158
Gaithersburg, MD 20899
USA

One final point, I have been collaborating with a colleague in academia on the development of a technique for the measurement of retinol/RBP at very low concentrations (<pM) in a very small volume of blood (<μL). We feel this technique has great potential in population surveys since there is no sample preparation, blood volume is low, and analysis time is ~5 min. However, there is some additional research involved to prepare the method for mainstream use and we are looking for sources of funding. Are there any groups involved in international work with vitamin A that offer funding for basic research leading to improved methods of assessing vitamin A status? If so, we would be excited to hear from them.

Neal E. Craft, Ph.D. Biologist
Organic Analytical Research Division Chemicial Science and Technology Laboratory
National Institute of Standards and Technology, Gaithersburg, MD 20899, USA

NEWS AND NOTES

Sight and Life vol 7, no 2, December 1992 (Task Force "Sight and Life", F. Hoffmann-La Roche Ltd, PO Box CH-4002 Basle, Switzerland

Mr. Tryson C. Ngalande on "Eye care services in Zambia" who was supported by a Sight and Life scholarship for the Course in Community Eye Health 1991/2 at the Institute of Ophthalmology, University of London. (Ed. Xerophthalmia is especially a problem in the Luapula Valley and interested readers should write to Mr. Ngalande, Zambia Flying Doctor Service, Ndola Airport, Box 71856, Ndola, Zambia).

Ghana VAST, Vitamin A Supplementation Trials (Maternal and Child Epidemiology Unit, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT). Two reports: Child Health Study — report of activities April-March 1992; Survival Study report of activities April 1991-March 1992.

Vital News vol 3, no 2 from Vitamin A Field Support Project (1616 N Fort Myer Dr., Suite 1240, Arlington, VA 22209, USA). This issue is primarily devoted to vitamin A deficiency in Africa where WHO has identified 18 countries where vitamin A deficiency has either been documented or is suspected to be a public health problem. (see also Publications Review).

Action Health 2000 (The Gate House, 25 Gwydir Street, Cambridge CB1 2LG, UK). The latest circular letter describes how they have "moved from being a volunteer sending agency to a development agency whose emphasis is on transferring health care skills".

International Health Exchange (Africa Centre, 38 King Street, London WC2E 8JY UK) "aims to promote understanding of health care and its delivery in developing countries in the context of primary health care; to provide a forum for health workers, non governmental organisations and others to communicate viewpoints and experience on issues and practical approaches to health development; to act as a resource for information on training and work in health development". The Health Exchange is a 20-page bulletin appearing bimonthly and is a health development and jobs magazine and a programme of short training courses on primary health care, surgery and refugee community health.

AHRTAG (Appropriate Health Resources and Technologies Action Group Ltd) — 1 London Bridge Street, London SE1 9SG, UK, has published "Resources list of free international newsletters" 1992/3 edition. Details are given of 110 newsletters (of which the Xerophthalmia Bulletin is one) free of charge to readers in developing countries. They cover a wide range of primary health care related issues including disease control, AIDS, mother and child health and health education, and are indexed by subject, language and geographical focus.

AHRTAG also publishes a new bulletin, Health Action, no 2 September 1992. It carries an interesting section entitled Global Scandals, including a section on the growing gap between the rich and the very poor. Even in the U.S. about one in four of the population does not have proper access to health care because of the rising costs of health insurance.

Nutrition Society: Task Force on Overseas Members (10 Cambridge Court, 210 Shepherds Bush, London W6 7NJ, U.K.) has produced an information sheet on low-cost newsletters and bulletins covering international nutrition.

Find Your Feet — annual report and accounts 1991-2 (37-39 Great Guildford Street, London SE1 0ES). At the start of the year projects were running Bangladesh, India, Bolivia, Mexico and Nicaragua. During the year two new projects started in India, bring the total to 14.

Newsletter no 7, October 1992 also contains details of projects.

WHO Europe Nutrition Network (Nutrition Unit, WHO Regional Office for Europe, Scherfigsvej 8, 2100 Copenhagen, Denmark). Those who request to be put on the mailing list receive regularly information concerning the many activities of this network, including documents currently available and meetings — forthcoming is "Current research into eating practices", October 14-16, 1993, Potsdam, Germany, for details write to AGEV e.V., Postfach 10 01 06, D-W-8200 Rosenheim, Germany.

IAPB News no 17, December 1992 (International Association for the Prevention of Blindness, c/o Sight Savers, PO Box 191, Haywards Heath, West Sussex RH16 4YF, UK).

NFI Bulletin, vol 13, no 4, October 1992 (Nutrition Foundation of India, B-37, Gulmohar Park, New Delhi, India). Includes articles on food safety and quality; variations in food consumption patterns; and nutrition and the environment.

Nutrition News, vol 13, nos 3 and 4, July and October 1992 (National Institute of Nutrition, Tarnaka, Hyderabad 500 007, India). Include articles on nutrition training in community settings and diabetes mellitus and vitamin D.

NCP Bulletin, January-March 1992 (Nutrition Center of the Philippines, PO Box 1858, MCPO, Makati, Metro Manila, Philippines). The main feature tells of the work of a female private doctor with Quezon City health staff on a health and nutrition programme for the urban poor. Among other deficiences 1.7% of the children were found to have night blindness. Stress was laid on health promotion and it is hoped that some benefits will continue after the cessation of the project in December 1991.

Contact, a bimonthly publication of the Christian Medical Commission, World Council of Churches, 150, route de Ferney, 1211 Geneva 2, Switzerland. Nos. 125 and 6, June and August 1992 targeting subjects — Retraining doctors for community medicine to meet the health needs of the majority; and AIDS: a community commitment.

Mothers and Children, vol 11, no 2 1992, American Public Health Association, 1015 15th Street, NW; Washington DC, 20005, USA. Published 3 times a year in English, French and Spanish

Essential Drugs Monitor, no 13, 1992 from WHO, CH-1211, Geneva 27, Switzerland.

Dialogue on Diarrhoea, issue no 50, September 1992 from AHRTAG, 1 London Bridge Street, London SE1 9SG.

On the Line, newsletter of International Medical Corps, Fall 1992, vol 7, no 1 (5933 West Century Boulevard, Suite 310, Los Angeles, CA 90045, USA). Over the last 8 years IMC has provided health care and training to people in seven countries, such as Somalia, Cambodia and Bosnia.

Learning for Health, twice yearly bulletin with articles on education methodology, communication strategies, curriculum development, and health education programmes (Education Resource Group, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA, UK).

Safe Motherhood, newsletter published three times a year, free in English and French from Division of Family Health, WHO, CH 1211, Geneva 27, Switzerland.

Programme for Control of Diarrhoeal Diseases, update nos 11 September and 12 November 1992 (WHO, Geneva). Topics covered are Towards rational use of drugs in the management of diarrhoea in children; and Advising mothers on management of diarrhoea in the home.

International Journal of Food Sciences and Nutrition — a new quarterly journal. The editor especially welcomes the submission of suitable manuscripts from developing countries — for a free sample copy and more information contact the editor, Dr. CJK Henry, School of Biological and Molecular Sciences, Brookes University, Oxford OX3 0BP, UK.

Public Health Nutritional Epidemiology — 5th European Postgraduate Summer Course, June 21-July 9, 1993 — contact Lorna du Lac, Course Administrator, Department of Human Nutrition, University of Southampton, SBS Building, Bassett Crescent East, Southampton SO9 3TU, UK. (Fax: 0703 594459).

Mr. Dennis Burkitt, in January 1993 received the Bower prize, valued at $373,000, the largest American award for the achievement of science from The Franklin Institute, Philadelphia for his research work on Burkitt's lymphoma and dietary fibre.

Professor M. Q-K Talukder, has been appointed as Project Director and Professor of Paediatrics, Institute of Child and Mother Health, Dhaka, Bangladesh.

W. Henry Sebrell, Jr, MD, died at the age of 91 in September 1992. On qualifying in medicine he joined the U.S. Public Health Service and worked with Joseph Goldberger who discovered the cause of pellagra. Later he worked on deficiency of riboflavin and other B group vitamins. During the second world war he served as a consultant with the Army on the development of the field ration and was battle orders. In 1950 Henry Sebrell was appointed Director of the National Institues of Health. During his 5-year term the Clinical Centre was opened and the extramural research grants programme was instituted. In 1957 he founded the Institute of Nutrition Sciences at Columbia University, New York and in 1962 with a substantial research grant from the NIH the Nutrition Research Programme in the School of Medicine at the American University of Beirut was started. I had the privilege of serving as its director from the beginning until it had to be terminated because of the civil war in Lebanon in 1976. Henry proved to be a deeply wise colleague and over the years of close association became a trusted and greatly valued friend. Through his many-faceted career Henry Sebrell has left a permanent impression upon nutrition as applied to medicine and public health. Ed.

Jean Mayer PhD the French-born nutritionist has died in Florida at the age of 72. He was born into a distinguished medical family. He had a notable career during the second world war, being a prisoner of war and escaping, working for British intelligence and receiving no less than 14 military decorations. After becoming an American citizen he was a professor at Harvard from 1950-75 where he researched the causes of obesity and did extensive work on malnutirition in Africa and Asia. Since 1976 he had been president of Tufts University whose international standing he had greatly helped to enhance.

LITERATURE DIGEST

A new spectrophotometric assay for the determination of vitamin A and related compounds in serum. Internat J Vit Nutr Res 1992; 62:221-7 Oliver RWA and Kafwembe EM (Biological Materials Analysis Research Unit, Department of Bilogical Sciences, University of Salford, Salford M5 4WT, UK and Tropical Diseases Research Centre, PO Box 71769, Ndola, Zambia). 'A new, direct multicomponent spectrophotometric assay for determining the vitamin A, lycopene, the total b-carotene + b-cryptoxanthin, the total lutein + a-carotene content of human serum is reported. The new method has been validated by performing parallel HPLC assays and is likely to be especially useful for use in population screening programmes. It is also suitable for screening paediatric samples'.

Abnormal T-cell subset proportions in vitamin A-deficient children. Lancet 1993; 341:5-8. Semba RD et al, Dana Center, Wilmer Institute, Johns Hopkins Hospital, Baltimore, MD 21287-9019, USA. In 55 children aged 3-6 years, 30 with xerophthalmia and 25 normal, CD4/CD8 ratios and proportions of circulating CD4 naive, CD4 memory, CD8, CD45RA, and CD8, CD45RO T-cell subsets were measured. Significant differences were found between the two groups in relation to these subsets of T-cells. The

found were reversible by vitamin A supplementation.

Vitamin A and infant immunity. Lancet editorial. 1993; 341:28 Bates CJ reviewing the above paper points out that vitamin A is known to have numerous effects on different aspects of the immune process. (Ed. not capable of quantitative measurement yet is also the known damage to the integrity of epithelial cell barriers which must be presumed to be of key significance in the body's resistance to invading pathogens).

Efficacy of massive doses of retinyl palmitate and mango consumption to correct an existing vitamin A deficiency in Senegalese children. Br J Nutr 1992; 68:529-40, Carlier C et al. Institut National de la Sante et de la Recherche Medicale (INSERM), Unite 56, Hopital de Bicetre, 78 Ave de General Leclerc, 94275 Le Kremlin-Bicetre, France. 220 Senegalese children aged 2-7 years were examined before and after vitamin A supplementation and also in relation to intake of beta-carotene from mango. Conjunctival impressions were taken. Not all those with abnormal cytology showed reversal to normal after vitamin A alone. It was suggested that a lack of retinol-carrier proteins might be responsible and that dietary beta-carotene might be effective.

Transfer and metabolism of retinol by the perfused human placenta. Pediatric Research 1992; 32:195-99. Dancis J et al, New York University Medical Center, 550 First Avenue, TH 528, New York, NY 10016, USA. An in vitro perfusion system was used with independent maternal and fetal circulations. It was concluded that RBP binding reduces the accumulation of retinol in the placenta and the transfer to the fetus, that retinol is transferred intact to the fetal circulation where immediate binding is not to RBP, and that redistribution to RBP occurs subsequently, possibly in fetal liver.

B-carotene and a-tocopherol are synergistic antioxidants. Archives Biochem Biophys 1992; 297:184-7. Palozza P and Krinsky NI, Department of Biochemistry, Tufts University School of Medicine, Boston, MA 02111-1837, USA. 'The possibility of a cooperative interaction between fat-soluble antioxidants is examined in a membrane model. A combination of B-carotene and a-tocopherol results in an inhibition of lipid peroxidation significantly greater than the sum of the individual inhibitions. Our data provide the first evidence that B-carotene can act synergistically with a-tocopherol as an effective radical-trapping antioxidant in membranes'.

Vitamin A levels in children with measles in Long Beach, California. J Pediatr 1992; 121:75-8. Arrieta AC et al Dept. of Pediatrics, Children's Hospital of Orange County, 455 S Main St., Orange, California 92668, USA. 20 children with measles and a similar number in a well control group were studied. It was found that half of the measles group had serum retinol levels less than 0.7 mmol/L, none of those in the well group had such a level. These results 'support evaluation of vitamin A status as part of acute management of measles in the United States'. (Ed. These workers are apparently unaware that it has been repeatedly shown that serum retinol levels drop, often markedly, in the acute phase of a childhood febrile illness and especially in measles. In other words these levels cannot be used to assess vitamin A status under these circumstances).

Corneal ulceration in Tanzanian children: relationship between measles and vitamin A deficiency. Foster A and Yorston D. Tran Roy Soc Trop Med Hyg 1992; 86:454-5 also Corneal ulceration in Tanzanian children: relationship between malaria and herpes simplex keratitis, TRSTMH 1992; 86:456-7 and Herpetic keratitis in Tanzania: association with malaria. Brit J Ophthal. 1992: 76:582-5. ICEH, Institute of Ophthalmology, Bath Street, London EC1V 9EL, UK. At a hospital in central Tanzania eye disease in young children was studied in two 3-year periods, 1982-4 and 1986-8. 189 cases of corneal ulceration were identified. Those attributable to vitamin A deficiency fell from 23.4% to 7.3% and was attributed to improved measles immunisation coverage. On the other hand herpes simplex keratitis increased over the same periods from 35.5% to 65.8%. The cases were most common from February to May and this is also the peak season for malaria. The increased incidence may have been related to the increasing prevalence of chloroquine-resistant malaria in Africa. (Ed. Once again such simple hospital-based studies, carefully planned and executed, illustrate how data of great practical significance can be collected quite easily. Not only may a problem not previously recognised have attention drawn to it, but as in this case, the changing pattern of disease may be revealed and the efficacy of an immunisation programme on the one hand and the threat of increasing chloroquine resistance on the other be highlighted for further investigation).

Separation and identification of carotenoids and their oxidation products in the extracts of human plasma. Anal Chem 1992; 64:2111. Khachik F et al, USDA, ARS Beltsville, Human Nutrition Research Center, Beltsville, MD 20705, USA.

Mothers' and children's intakes of vitamin A in rural Bangladesh. Amer J Clin Nutr 1992; 56:136-47. Zeithlin MF et al School of Nutrition, Tufts University, Medford MA 02155, USA. The vitamin A intake of 370 mothers and 183 children 3-27 mo was ascertained from January to July in 1986. For mothers the most important source was vegetables and intake was not related to wealth or any other socioeconomic factor. Breast milk and seasonally available mangoes provided most children with close to 100% of the RDA

However, fourteen children who had stopped breast feeding were at very high risk of deficiency. (Ed. It is not clear why the study was confined to only 6 months of a year, it would also have been useful to learn the intake of fat and some other related nutrients).

Distribution of orally administered b-carotene among lipoproteins in healthy men. Amer J Clin Nutr 1992; 56:128-35. Johnson EJ and Russell RM USDA Human Nutrition Research Center on Aging at Tufts University, 711 Washington Street, Boston MA 02111, USA. Plasma concentration increased by 6h postdosing and peaked at 24h and returned to baseline by 7d; suggesting homeostatic control. Intestinal input accounts for early rises in circulating concentrations whereas hepatic secretion is the source of late increases.

Sex differences in postabsorptive plasma vitamin A transport. Amer J Clin Nutr 1992; 56:911-6. Johnson EJ et al address as above. 'the present study provides evidence that the pathogenesis of coronary heart disease among men in general, and older men in particular may be related to delayed clearance of intestinal lipoproteins'.

Studies on the application of the relative-dose-response test for assessing vitamin A status in older adults. Amer J Clin Nutr 1992; 56:543-7. Bulux J et al. reprint requests to R.M. Russell address as above. The maximum plasma response was at 6-7h after dosing compared with 5h in younger subjects. The diagnostic concordance of two RDR tests at 7d intervals was 71% and linear regression of the two RDR values gave a correlation coefficient of -0.08. It was concluded that in subjects over 60y multiple repetitions of the test would br required to provide a stable indication of vitamin A stores.

Effect of b-carotene supplementation on photosuppression of delayed-type hypersensitivity in normal young men. Amer J Clin Nutr 1992; 56:684-90. Fuller CJ et al. reprint requests D.A. Roe, Room 108 Savage Hall, Cornell University, Ithaca, NY 14853, USA. DTH test responses were significantly suppressed in a placebo group after UV treatment. Suppression was inversely related to plasma b-carotene concentrations. There was no significant suppression of DTH test responses in the b-carotene group.

Cross-sectional study on the iron and vitamin A status of pregnant women in West Java, Indonesia. Amer J Clin Nutr 1992; 56:988-93. Suharno D et al. reprints not available. Of 318 normal pregnant women studied 49.4% were anaemic and according to multiple criteria 43.5% had iron deficiency anaemia, 22.3% had iron deficient erythropoiesis, and 6.6% had iron depletion. Serum retinol showed 2.5% were deficient and 31% had marginal status. On a subgroup RDR test showed 8.9% had deficient vitamin A stores. After adjusting gestational age, parity, and subdistrict serum retinol was positively correlated (p less than 0.01) with Hb, Hct and serum Fe.

The cost of successful adolescent growth and development in girls in relation to iron and vitamin A status. Amer J Clin Nutr 1992; 55:955-8. Brabin L and Brabin BJ Liverpool School of Tropical Medicine, Pembroke Place, Liverpool L3 5QA, UK. A review of the literature.

India: Advertising of infant foods to be restricted. Lancet 1992: 340 Parkash P. The Indian parliament has passed after a long and interrupted passage a bill which, when it comes into force, will severely restrict the advertising and promotion of baby products. In essence it incorporates the contents of the International Baby Food Code adopted by WHO in 1981, but expands its scope to include infant foods. The market for baby foods is growing at a rate of about 6% per year. At present the £180 million market is almost entirely shared between Amul, the manufacturing unit of highly successful Indian milk cooperative venture and Nestle. The law makes food inspectors responsible; they are overworked and often corrupt. The bill makes illegal the use of the health system or its employees for promotion of these products but there is no agency to monitor this. The majority of working women in the country do so in the unorganised sector where maintenance of breast feeding is not provided for.

Breast feeding and HIV infection. Brit Med J 1992; 305:788-9. Cutting WAM, Department of Child Life and Health, University of Edinburgh, EH9 1UW, U.K. Breast milk may transmit HIV to the child and the risk has been calculated as about 1 in 4. However, in many poor communities not to breast feed may be a death sentence for the infant. The most recent WHO recommendation states 'where the primary causes of infant deaths are infectious diseases and malnutrition breast feeding should remain standard advice given to women, including those who are know to be HIV infected'.

Misconceptions on nutrition of refugees. Lancet 1992; 340:1345. Mason J et al WHO, 1211 Geneva 27, Switzerland. Six misconceptions are listed and explained — 1. starving people can eat anything: 2. children with diarrhoea should not be intensively fed; 3. refugees can manage with less; 4. trading foods indicates that people do not need all the rations; 5. a standard ration is sutiable for all populations; and 6. energy adequacy means nutritional adequacy. These and other issues are being addressed in collaborative inter-agency revision of the 1978 manual 'The management of nutritional emergencies in large populations' to be published soon by WHO.

XEROPHTHALMIA CLUB BULLETIN

No. 53

JULY 1993

Supported by Sight Savers (Royal Commonwealth Society for the Blind) and the International Vitamin A Consultative Group

Bulletins are *sent free* to anyone seriously concerned with xerophthalmia
Please apply for membership to the Editor

VITAMIN A AND ENTRAPMENT

In 1990 Dr. Maurice King wrote a paper entitled *Health is a sustainable state*[1] which aroused considerable controversy[2], chiefly because of the view he expressed that in some circumstances it would be right not to introduce "such desustaining measures as oral rehydration on a public health scale". King has much firsthand knowledge of third world problems, wrote the influentual book *Medical care in developing countries* in 1966[3] and his opening chapter 'Medicine in an unjust world' to the Oxford Textbook of Medicine[4] attracted much attention. Recently King has struck again[5] and fuel has been added to the fire by correspondents[6]. The concept of 'entrapment' is central to the argument. It is stated that large segments of the populations of many developing countries have reached, or soon will reach, this state of entrapment. This arises when pressure of population outstrips the carrying capacity of the related ecosystem, resulting in a fall of welfare standards to an unacceptable level and a rising mortality rate. There are only three possible outcomes: people migrate — usually to swell the urban slums, they hope to be supported indefinitely by outside aid, or they die where they are. King challenges aid agencies, especially those of the United Nations system, to face up to the ethical dilemma posed by entrapment. The 'legitimate double-think' in the title of his recent paper refers to his view that 'political tensions surrounding entrapment are at present so great that agency executives must not be pressured to recognise it' while the rest of us must do so.

At not time has the impact of vitamin A supplementation on young child mortality been brought into this debate. I have hesitated to raise the issue in these pages for quite some time but now, in addition to King's re-entry into the ring for a second round, there are several recent events which oblige the vitamin A community to face up to making a stark choice.

1. To date there have been four separate, although overlapping, meta-analyses of the impact of large dose vitamin A intervention on child mortality[7]. All are agreed that there is about a 30% reduction in mortality.
2. The magnitude of the saving of life if such a measure were fully implemented has been estimated to be of the order of 1.3-2.5 million of the nearly 8 million deaths of under 5-year-olds that occur each year in those countries that are known to have the highest risk of vitamin A deficiency and xerophthalmia[8].
3. On the basis of the Bellagio findings UNICEF in its most recent report[9] has accepted the validity of the effect of vitamin A supplementation and has concluded "There is no longer any reason to wait. Vitamin A supplements have taken their place alongside the handful of other low-cost strategies that could now significantly reduce illness and death among the children of the developing world".

All of this greatly strengthens King's argument in one sense, it adds more grist to his mill, more supporting data. It does not, of course, help any of us in our agonising attempts to make up our minds whether or not we would be in favour of universal and continued administration of vitamin A to all children at risk of vitamin A

status-related mortality. I do not intend to adopt a position here — I encourage you to do so in these columns in subsequent issues. If possible you should first read King and his supporters and critics in the original (hence the references). I shall only make three additional points.

(i) It has often happened that once dosing with vitamin A becomes routine a dramatic fall in efficiency over time renders a programme ineffective[9]. This is no reason for it not being done. If immunisation can be made efficient and UNICEF says vaccines now regularly reach 80% of the world's infants, so can vitamin A supplementation, especially if added to immunisation services[10].

(ii) King's thesis is based to a considerable extent on mortality data. It is not generally appreciated how 'soft' most of these data for developing countries are. UNICEF for example makes it very clear that in its publications 'most of the U5MR (under 5 mortality rate) and IMR (infant mortality rate) are interpolations based on five-year estimates'. Anyone tempted to use these mortality data as if they were graven on stone should read Murray's searching analysis of their true nature and the quite bizarre mental gymnastics gone through for their production[11].

(iii) The whole idea of sustainable this that and the other is very popular just now. It is argued that if we could exploit nature in a sustainable way the depletion of the earth's resources would be halted. Although the principle is fine the problem lies in its practice. It is man that needs to be managed. including curbs on population growth, not resources. Unfortunately history shows that man makes a mess of just about everything he tries to control[12].

References

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2. Lancet letters 1990, 336: 659-60; 936-8; 1312-3; 337: 50-1; 307-8: 339: 377-8.
3. King M. Medical care in developing countries. OUP 1966.
4. Oxford Textbook of Medicine. Eds. Weatherall, Ledingham and Worrell, OUP 1983.
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6. Lancet letters 1993: 341: 1026-8.
7. Lancet 1992; 339: 864; Brit Med J 1993; 306: 366-70; J Amer Med Assoc 1992; 269: 989-903: IVACG Meeting, Arusha, 1993.
8. Humphrey J.H. et al Bull Wld Hlth Org 1992; 70: 225-32.
9. West K.P. and Sommer A. IVACG Report 1984.
10. UNICEF, State of the World's Children 1993.
11. Murray C.J.L. A critical review of international mortality data. Soc Sci Med 1987; 25: 773-81.
12. Ludwig D. Hilborn R. Walters C. Uncertainty, resource exploitation, and conservation: lessons from history. Science 1993; 260: 17.

D.S. McLaren

COMPREHENSIVE VITAMIN A PROGRAMMES WERE FOCUS OF RECENT XV IVACG MEETING

Integration of vitamin A interventions into existing primary health care and food-based strategies unites commitment with action, according to participants at the recent XV IVACG Meeting in Tanzania. "We must seize the global momentum to virtually eliminate vitamin A deficiency", said Dr. Abraham Horwitz, chairman of the International Vitamin A Consultative Group (IVACG) as he opened the XV IVACG Meeting.

Representatives from 51 countries were among the 294 policy makers, implementors, and scientists in health, nutrition, agriculture, and development participating in the meeting, held 8-12th March, 1993 in Arusha, Tanzania. Throughout the five-day programme numerous speakers presented research concerning progress in changing dietary behaviours related to vitamin A, newer methodologies for assessing subclinical vitamin A deficiency, consequences for human health and disease, and physiological functions of vitamin A.

Several speakers presented evidence of substantial gains in meeting the goal of virtual eradication of vitamin A deficiency. A significant outcome is the reduction in childhood mortality from infections. The impact of vitamin A supplementation on mortality appears to be due to a reduction in the severity of infection rather than in the incidence of infection. Others referred to 'missed opportunities' in linking vitamin A with health care delivery systems such as immunization services and growth-monitoring programmes. These are the 'windows of opportunity' for the future. A comprehensive approcah to preventing vitamin A deficiency combines short-term strategies such as vitamin A capsule distribution with dietary diversification, a long-term strategy. Factors identified as essential for a successful vitamin A programme include adequate political will; effective surveillance to guide policy formulation, programme design, and implementation; and flexible training, supervision, and management systems.

In closing the meeting, Dr. Horwitz stated, "The reduction of poverty, although essential, is not a prerequisite for the elimination of vitamin A deficiency. The process to reach this gaol should start or be strengthened, and the sooner the better. The persistence of vitamin A deficiency anywhere in the world is cruel, because it exposes mothers and children to great risks. It is immoral, because it ignores basic human values. It is unacceptable, because it can be prevented".

A complete report of the meeting will be available from the IVACG Secretariat, 1126 Sixteenth Street N.W., Washington, D.C. 20036, USA.

With support from a cooperative agreement between the Nutrition Foundation, Inc. and the Office of Nutrition, Bureau for Research and Development, U.S. Agency for International Development, the IVACG Steering Committee and Secretariat organized the meeting with a local committee in Tanzania. Other organizations, include bilateral agencies, United Nations agencies, and the food industry, provided addtional support. IVACG was establised in 1975 to guide international activities aimed at reducing vitamin A deficiency in the world. IVACG strongly supports the goal of virtually eliminating vitamin A

deficiency by the turn of the century. The XV IVACG Meeting provided a forum for exchanging new ideas and important research findings, encouraging innovation, and promoting action programmes to help reach the goal. A fuller account of the meeting is available from *Sight & Life* (see page 6).

LETTERS

200,000 I.V. Vitamin A Capsules. It has taken four years for our Chief Pharmacist to obtain a small amount of vitamin A capsules, although the importance of this vitamin in preventing blindness in malnourished children and its benefit in many other infections is recognised worldwide.

A small batch of soft gelatin capsules was made available to our hospital after receiving special permission from the S.A. Medicines Control Council to use this unregistered product.

It appears that the importance of this vitamin is not understood by many doctors and nurses even those working amongst disadvantaged communities, and it is not mentioned in some local PHC books. Unless there is a demand for it, the pharmaceutical company concerned will never produce the capsules or drops which are so vital for so many of our children.

A.O. Pugh, Specialist (Community Health)
Tintswalo Hospital, R.S.A.

From Dr. J. Gmünder, Sight & Life. It is difficult for me to understand the meaning of Professor John Hansen's statement regarding withdrawal of the 2000,000 vitamin A capsules. These capsules have never been a Roche sales product, so, how could they been withdrawn?

There is no change of policy at *Sight & Life* either. We continue to donate the 200,000 vitamin A capsules to various organizations at a level of 2-3 million per year. As you know these capsules are specially manufactured for the purposes of *Sight & Life* to comply with the standard for high-dose vitamin A capsules as defined by UNICEF.

Further to the information given in my letter dated March 9th, I can share with you the following details passed on to me during my recent trip to South Africa.:

(a) *still available* are the following Roche preparations:

— 2 ml ampoules, containing 100,000 IU vitamin A per ml
— sugar coated chewable tablets, containing 50,000 IU vitamin A per tablet

(b) *recently withdrawn* from the market:

— Arovit drops with 150,000 IU vitamin A per ml

PUBLICATIONS REVIEW

Nutrition for Developing Countries (1993): Savage King, Felicity & Burgess, Ann. Oxford: Oxford Medical Publications; also in a Low Cost Edition (subsidised by the British Government) 462 pages.

The updated 'Nutrition for Developing Countries' is bigger and better than before. It is still very relevant to developing countries, particularly because of the many practical examples. It is encouraging to reflect that there has been an increase in knowledge and experience of nutrition, even in the developing countries, where problems can seem so difficult to solve.

The authors still write for 'front line' workers, mainly as well as their teachers and trainers. For the first time they also address physicians in a chapter on 'Severe Protein Energy Malnutrition'. The extended scope recognises the fact that this may be the sole text in a hospital or health centre.

Primarily the level is simple. Simplicity without loss of meaning is very difficult to achieve. We congratulate the authors on an immensely readable book and especially on the clear explanations of difficult key concepts in nutrition science. Particularly striking examples are the clear text and excellent pictures which illustrate food energy and nutritional bulk and energy requirements (chap 2), protein requirements (chap 3), and iron availability (chap 4 p37). This is a unique achievement which should attract a wide readership. A small 'nitpick': we were unhappy with the way the idea of 'incomplete proteins' perpetuates the categories of 'first' and 'second' class proteins and replaces the idea of 'limiting amino acids'.

This book is mainly for people who want to do and not merely to know something about nutrition. Teaching and learning are helped by the many case studies, illustrations and sections of 'Things to Do' at the end of each chapter. The appendices are useful resources for present and continuing learning. The book is in harmony with the current concepts used by the international agencies and the big NGO's. We particularly liked the chapters on 'Breastfeeding', 'Starting Other Foods' and 'Working with Communities'. There is something for everyone — 'Undernutrition' (in children and in adults), 'Vitamin A Deficiency', 'Nutritional Anaemias', 'Improving Gardens', 'Food Security' and 'Training for Nutrition' and much more.

Rich in the experience of East Africa, could it be for all developing countries? No one text can be comprehensive, of course. There is a risk that readers may be put off when they do not recognise their names or places. The more relevant the examples, the easier for them to grasp and apply the information. There is another risk that foods or practices which are mentioned gain credibility while those that are left out may lose credibility. Many examples of local fruits are given (eg p36). Small animals that can be neglected, like mice pictured on p55 and insects are mentioned, deservedly. It is a pity that the same detail was not extended to other types of food which are the subject of nutrition messages: anonymous green leafy vegetables could include Amaranths, pumpkin leaves, bean leaves; small fish (p33) could be named, like, lapenta, chambo or tilapia, and included in the section on foods (chap 5). It

would have been helpful if the book had highlighted the nutritional roles the wild foods mentioned on p55 play in the dry seasons in Sub-Saharan Africa, when food may be scarce.

If the starchy fruits, roots and tubers, are eaten fresh, or boiled or as porridge, as shown in the diagram on p47. they are indeed bulky. Cassava, plantain and sweet potato can be useful snack foods when they are eaten roasted, baked or fried, as snacks. We think the picture to show that drying maize cobs (p69) properly prevents mould, conveys a useful message but would have preferred one which showed the food on a raised platform to prevent contamination, like the picture of sundrying fish on p57. This is certainly in keeping with a message extension workers in East, Central and Southern African countries now promote.

There are many different food groups in use in different countries – 6 or 7 in the Caribbean; 3 in Malawi and 4 in Zimbabwe. Chapter 8 is excellent for the more universal 'mixed meal' concept, the illustrations of varying portions for different ages and how snack foods help to ensure that energy needs are met.

These concerns are relatively minor, and are anticipated by the authors' preface. Like the authors, we hope that teachers, trainers and programme managers will publish the materials, guides or manuals they devise and use, in addition to this book, to suit their own circumstances. Meanwhile, there is something to suit almost anyone connected with nutrition, health and community development programmes in *Nutrition for Developing Countries.*

Jackie Landman and Mabel Chiligo
Department of Human Nutrition, University of Southampton

Rapid Assessment Procedures. Qualitative Methodolgies for Planning and Evaluation of Health Related Programmes eds. Nevin S. Scrimshaw and Gary R. Gleason 1992 International Nutrition Foundation for Developing Countries. Boston MA, USA. No price.

This 528 page volume is the proceedings of an international conference held in Washington, DC in 1990. Unless the reader has already been acclimated to the acronym RAP (Rapid Assessment Procedures) and the related RRA (Rapid Rural Appraisal) out of which the former grew, it may take some time and effort to find one's reading feet.

In essence this is all about a movement over the past decade or so that has sought to apply the qualitative sources of information long familiar to anthropologists (in addition to, rather than in place of, the more quantitative and statistical sources of many social scientists derived often from lengthy and impersonal questionnaires) in community interventions. There is nothing special about their use in nutrition or even in health but the interests of the senior editor and others guides it this way and most of the papers have this flavour.

A quotation on p15 puts what is regarded as the ideal approach rather well – "the quantified bones of the survey with the qualitative flesh of quick assessment studies'. One disappointing aspect of this collection of papers is that very few give detailed data of their findings in the studies that have been carried out. A notable exception is that undertaken by Wilson, Shale and Parker (pp185-204) in Lesotho to assist in planning for the control of ARI (Acute Respiratory Infections) in children. In the present context it is unfortunate that the topic is unrelated to nutrition.

The reviewer is left largely unconvinced of the utility of RAP by this particular presentation. Detailed and fully documentd accounts of just a few studies in which its efficacy was clearly demonstrated would have been much more persuasive than this voluminous material largely failing to get to grips with the subject.

Experience has repeatedly shown that a well-trained and enquiring mind, with the possibility of operating fully in a particular situation, is unparalleled in its capacity to arrive at the truth. In just this way Lind with scurvy, Eijkman with beriberi and Goldberger with pellagra and others laid the foundations of our knowledge of dietary deficiency diseases. In more recent times Cicely Williams discovered the dietary origin of kwashiorkor and Dennis Burkitt demonstrated the nature of the lymphoma named after him and also the importance of dietary fiber as a result of meticulous observation and thought over prolonged periods of time spent in treating the sick. As a very young research worker I came to accept the wisdom of my professor's aphorism "all that you require for success is running water and one idea". There is a great deal of perspiration here and precious little inspiration.

Donald S. McLaren

Vitamin A and Breastfeeding. A comparison of Data from Developed and Developing Countries, 1933 by Vicky Newman, Wellstart, 4062 First Ave., San Diego, CA 92103, USA. pp 112.

A very comprehensive and uptodate review of vitamin A status and lactation. In developing countries 'improving the vitamin A status of lactating women, promoting the use of colostrum, encouraging exclusive breastfeeding for four to six months of life (Ed. but see next item) and the addition of appropriate vitamin A-rich weaning foods after that time while breast-feeding continues, are important strategies for improving vitamin A status of infants and young children'.

A limited number of copies are available without charge: requests from developing countries should be sent to APHA Clearinghouse on Infant Feeding and Maternal Nutrition, 1015 15th Street NW, Washington, DC 20005, USA; request for developed countries should be sent

to Wellstart International, 4062 First Avenue, San Diego, CA 92103, USA.

Recommended Length of Exclusive Breast-feeding, Age of Introduction of Complementary Foods and the Weanling Dilemma by Chessa Lutter, Research Advisor, Wellstart International. WHO, Diarrhoeal Disease Control Programme 1992.

A review and evaluation of the existing literature came to the following conclusions: there is scientific evidence for the following assertions:
1. Introduction of complementary foods to exclusively breast-fed infants increases the risk of diarrhoea;
2. Exclusively breast-fed infants have a pattern of growth that is different from that of formula-fed infants;
3. Current recommendations for energy intake exceed the mean energy intake of exclusively breast-fed infants by about 15-20%.

There is however lack of evidence for some commonly held assertions:
1. Growth faltering in the first 6 months among breast-fed infants living in poverty has not been established;
2. In the first 6 months it has not been established that breast-fed infants given complements grow better than those exclusively breast-fed;
3. An overall negative effect of diarrhoea on growth during the 4-6 month period has not been established.
Much research is required in this important area.

The State of World Rural Poverty, by Idriss Jazairy, Mohiuddin Almagir and Theresa Panuccio. IT Publications 1933. £14.95.

This book is a massive study of 114 developing countries made by the IFAD (International Fund for Agricultural Development). More than one billion people, or 20% of the world's population, are officially described as being the abject poor — they cannot meet their basic requirements for food, clothing and housing and earn less than 1$ US/ day. The number increased by 88m between 1986 and 1990 according to the World Bank. Most of these people, the authors state, are smallholder farmers, landless peasants, artisans, fishermen, nomads and indigenous ethnic tribes, the bulk of whom live in rural areas (the mushrooming slums and shanty towns are ignored). The theme of this book is that these people have been systematically despised and displaced over the past 40 years in the name of development, as agriculture has been modernised and resources directed to building industry and urbanisation. As a result of its findings the IFAD argues for a complete reversal of attitudes with investments in infrastructure, social services and relevant technology biased in their favour.

Training Manual for Assessing Vitamin A Status by Use of the Modified Relative Dose Response and the Relative Dose Response Assays by Furr HC, Tanumihardjo SA and Olson JA, Department of Biochemistry and Biophysics, Iowa State University, Ames, Iowa 50011, USA. 1992. This manual, which was developed under the auspices of the VITAL programme of the International Science and Technology Institute, Inc. and of the Office of Nutrition, Bureau for Research and Development, U.S. Agency for International Development, is available without charge. In addition, the testing compound for the modified relative dose response assay, namely, 3, 4-didehydroretinyl acetate, is also available from the Vitamin A Research Group, Iowa State University, Ames, IA 50011, USA. The fax number is 1-515-294-4141. (Ed. a review of this important document will appear in the next Bulletin).

Protein-Energy Interactions pp437, 1993. Proceedings of a meeting in Waterville, NH, USA held in October, 1991 by IDECG. Copies available free from Secretariat of IDECG, % Nestle Foundation, PO Box 581, 1001 Lausanne, Switzerland. A very comprehensive and uptodate account of the subject. For the general audience summary statements and conclusions would have been helpful. From the short section on resarch needs it seems that the group considers that many areas require much more study. Many workers in this field have spent their whole careers with very little of positive value for human health to show for it. One suspects that inate variability and environmental diversity of humans have often been underestimated in the quest for over-precise definition of dietary needs.

McCance and Widdowson's "The Composition of Foods 5th edition — 2nd Supplement — Vegetable Dishes" 1992 £24.50 from Sales and Promotion Department, Royal Society of Chemistry, Thomas Graham House, Science Park, Milton Road, Cambridge CB4 4WF, UK.

McCance and Widdowson a scientific partnership of 60 years 1993 £19.95 from The Publications Officer, The British Nutrition Foundation, High Holborn House, 52-54 High Holborn, London WC1V 6RQ, UK.

Food, Diet and Economic Change Past and Present by Geisler C. and Oddy D.J. 1993 £35.00 Leicester University Press, 25 Floral Street, London WC2E 9DS, UK.

The Nyasaland Survey Papers 1938-1943. Agriculture, Food and Health edited by Berry V. and Petty C. 1993, £29.95. Academy Books, 35 Pretoria Avenue, London E17 7DR, UK.

NEWS AND NOTES

Sight & Life. Annual Report 1992 (supported by F. Hoffmann-La Roche Ltd. PO Box CH-4002, Basel, Switzerland). In 1992 this Task Force provided assistance for 61 different projects in 27 countries. Among the varied activities was provision of more than 2 million high dose vitamin A capsules for 35 intervention projects in 22 countries as well as vitamin A in bulk and for the dispenser system devised by Roche. Of special concern are the recent reports of widespread xerophthalmia in young infants in Yala, Pattanee, and Narathivat, three southern provinces of Thailand. Also an alarming increase in the number of xerophthalmia cases and child deaths from measles reported from Malawi and also neighbouring countries affected by the worst drought of the century. An order form comes with the report for request of various publications, some in languages other than English.

Helen Keller International. Annual Report 1992 (note change of address - 90 Washington Street, 15th Floor, New York, NY 10006, USA). Also Vitamin A News Notes, Spring 1993 a biennial publication. *Like Sight & Life*, HKI has been active in the drought-striken countries of southern Africa.

High potency vitamin A solution in a pump dispenser is now available from the UNICEF Supply Division (contact local UNICEF office). One full push of the pump dispenses 100,000 IU vitamin A. One pump comes with 12 bottles each containing 60ml equal to 100 pushes of 100,000 IU each.

In Bolivia a nationwide survey of vitamin A status and other health indicators has recently been carried out of 979 children aged 12 to 71 months in 6 urban and 21 rural sites among the most disadvantaged areas of the country. Eye signs did not reach levels suggestive of a public health problem. Serum retinol was below 30ug/dl in 48.3% (interpreted as marginal or subclinical deficiency) with 11.3% less than 20ug/dl (usually designated 'low') — of these the rates were 19.3% in the altiplano-high-altitude plains in the mountains - and 16.5% in the llano-low-lying plains of the Amazon basin. (Ed. These latter two rates exceed the 15% level for a public health problem recommended by PAHO in 1970. This recommendation is at variance with the one give by WHO in 1976 and reconfirmed in 1982 which is 5% of the study population with levels less than 10ug/dl. Other instances of this kind of confusion over interpretation of biochemical data are occurring quite frequently — see page 8 this Bulletin).

Vitamin A+ Sieve. January 1993 (Janet Glasman, Rodale Press Information Services, 33 E. Minor Street, Emmaus, PA 18098 USA). Semi-annual digest of the vitamin literature. Addresses of original papers are included, making reprint requests possible. The feature review in this issue by Martha Capwell and reviewed by two experts, Kenneth Simpson and John Erdman is on the very important subject of 'Preserving Vitamin A During Processing, Storage and Cooking'.

Child to Child Activity Sheets are a resource for teachers, and health and community workers. Sheet 3.2 is entitled *Looking after your eyes* — for further information contact Child-to-Child, Institute of Education, University of London, 20 Bedford Way, London WC1H 0AL, UK.

Community Eye Health bulletin no. 9, 1992 (ICEH, Institute of Ophthalmology, Bath Street, London EC1V 9EL, UK) and NFI BULLETIN (vol 14 no. 2, 1993 — Nutrition Foundation of India, B-37, Gulmohar Park, New Delhi, India) both highlight the problem of cataract and have a good deal to say about dietary factors in the aetiology. Like so many other intractable health problems existing evidence points to multifactorial causation and also multifaceted nature of the disease. The papers from India concentrate mainly on the production in experimental animals of biochemical changes in the lens by deficiency of various nutrients in the diet. The favoured hypothesis developed at ICEH is an association of age-related cataract with episodes in the past of severe diarrhoea. A mechanism is described whereby diarrhoea, dehydration and malnutrition might lead to enzyme inactivation in the lens and unfolding of lens proteins. There are difficulties in interpreting the data and one wonders whether the factor(s) responsible might not be something else to which people likely to suffer from very severe diarrhoea might be more prone. Cigarette smoking and prolonged exposure to ultraviolet light B appear to increase the risk of senile cataract. Several epidemioligical studies of habitual dietary intake of nutrients and subsequent cataract formation have suggested that a low intake of antioxidant nutrients like ascorbic acid, B carotene, vitamin E and selenium may play a part.

CONTACT: bimonthly publication of the Christian Medical Commission, World Council of Churches, 150, route de Ferney, 1211 Geneva 2, Switzerland; nos. 127-129. These issues all deal with aspects of Community-determined Health Development with accounts of experiences in this field from various countries of the third world. In issues 127 and 129 an extended interview is given with David Werner who is best known for his book *Where there is no doctor* - a village health care book, the new edition of which was reviewed in Bulletin 51, November 1992.

AHRTAG March 1993 Primary Health Care Course Directory 1993/4 Edition. Free in developing countries from Bronach McConville, AHRTAG, 1 London Bridge Street, London SE1 9SG, UK (Fax 071 403 6003). Action Health - issues 3 and 4, December 1992, March-May 1993. *Implementing primary health care worldwide.*

Mothers and Children Vol 11 no. 3, 1992 — published three times a year in English, French and Spanish, free in developing countries (Clearinghouse, American Public Health Association, 1015 15th Street NW, Washington, DC 20005, USA.

Nutrition News Vol 14, no. 1, 1993, National Institute of Nutrition, Tarnaka, Hyderabad/500 007, India. Devoted to marking the 75th year since the founding of the institute.

Action Health 2000 Review 1991-2 'Developing primary health care and training programmes in partnership with communities across the world'. During 1991-2 more than 40 professionals worked in partnership with 12 locally initiated projects in India, Tanzania and Zambia (Action Health, The Gate House, 25 Gwydir Street, Cambridge CB1 2LG, UK).

Essential Drugs Monitor no. 14, 1993 from WHO, CH-1211, Geneva 27, Switzerland. In this issue; newsdesk, quality assurance, national drug policy, rational use, research, recent publications.

Hamari Aankhen Vol 17, no. 1, 1993 Quarterly publication, mostly in English, of the National Society for the Prevention of Blindness, India (Room 115, Dr. R.P. Centre for Ophthalmic Sciences, AIIMS, Ansari Nagar, New Delhi-110 029, India). The Bellagio Declaration is reproduced.

Dialogue on Diarrhoea Issue no. 51, December 1992, published quarterly by AHRTAG, 1 London Bridge Street, London SE1 9SG, UK.

News on Health in Developing Countries Vol 7, no. 1, 1993 on Safe Motherhood from NU Editorial Office, ICH, University Hospital, S-751 8[illegible] Uppsala, Sweden.

WHO Collaborating Centres for Nutrition Newsletter no.3, 1992. From Nutrition Unit, WHO Regional Office for Europe, Scherfigsvej 8, 2100 Copenhagen, Denmark.

Leeds Course in Clinical Nutrition, 7-10 September 1993, particulars about this annual course from Mrs. Hilary L. Helme, Department of Continuing Professional Education, Springfield Mount, Leeds LS2 9NG, UK (Fax 0532 333240).

Hunger Research. Briefing and Exchange, 6th Annual meeting 14-15 April, 1993, details from World Hunger Program, Box 1831, Brown University, Providence RI, 02912, USA. Fax 401 863 2192 (Ed. This notice came too late for action this year, but is in good time for 1994!)

Dr. Claudio Schuftan has offered to send free of charge any of a series of papers he has written on Food, Hunger and Nutrition / Primary Health Care and Development (Box 40874, Nairobi, Kenya. Fax 2542 712190).

IDECG Annual Report 1992. A number of the issues considered by the International Dietary Energy Consultative Group are of interest to those involved with problems of malnutrition in children (from Dr. B. Schurch, Executive Secretary of IDECG, % Nestle Foundation, PO Box 581, 1001 Lausanne, Switzerland see also Publication Reviews.

Journal of Refugee Studies. Vol 6, 1993 - for full details contact Journals Marketing, Oxford University Press, Walton Street, Oxford OX2 6DP, UK.

Obituaries Within the past few weeks the nutrition community in Britain has suffered the loss by death of four scientists, all of whom were to varying extents involved in work in the third world. Robert McCance, FRS, formerly professor of Experimental Medicine at Cambridge died at the age of 94. With Elsie Widdowson, FRS he had carried out research of uniquely broad reach over a period of sixty years. This is to be celebrated at a conference on 29th June at the Royal College of Physicians in London and in a book (see page 5). Perhaps their most widely known publication is the Composition of Foods which has reached a 5th edition and a 2nd Supplement has just been published (again see page 5).
Denis Burkitt, FRS died at age 82 only a few weeks after he had been awarded the prestigious Franklin award in the United States (see Bulletin no. 52) for his identification of the malignant tumour of children in Africa (Burkitt's tumour - the first in man to be casually linked with a virus, the Epstein Barr virus, and shown to be carried by a mosquito) and the role of lack of dietary fibre in a number of degenerative diseases associated with a western lifestyle.
T.P. Eddy was director of medical services in west Africa before he was associated with the Department of Human Nutrition at the London School of Hygiene for nearly 20 years.
Erica Wheeler died suddenly last November. She had been at the London School for 25 years and was latterly head of what had become the Centre for Human Nutrition. Through students and consultancies she had been involved in nutrition work in many developing counries. Her death occurred just after she had arrived for a consultancy to INCAP.

LITERATURE DIGEST

Vitamin A supplementation in infectious diseases A meta-analysis. Glasziou and Mackerras, DEM. Brit Med J 306:366-70. (Department of Social and Preventive Medicine, Medical School, University of Queensland, Herston, Queensland, Australia 4006). Of 20 controlled trials identified, 12 trials were randomised trials and provided 'intention to treat' data: six community trials in developing countries, and three in very low birth weight infants. Combined results for community studies suggest a reduction of 30% in all cause mortality. Analysis of cause specific mortality showed a reduction in deaths from diarrhoeal disease (in community studies) by 39%; from respiratory disease (in measles studies) by 70%; and from other causes of death (in community

studies) by 34%. Reductions in morbidity were consistent with the findings for mortality, but fewer data were available.

Vitamin A supplementation and child mortality. A meta-analysis. Fawzi W.W. et al J Amer Med Assoc 1993; 269: 898-903. (Department of Nutrition, Harvard School of Public Health, 665 Huntington Avenue, Boston MA 02115, USA). All 12 vitamin A controlled trials with data on mortality identified in a search were used in the analysis. Vitamin A supplementation to hospitalized measles patients was highly protective. Supplementation was also protective against overall mortality in community-based studies.

Effectiveness of vitamin A supplementation in control of young child morbidity and mortality in developing countries. Beaton G.H. et al. XV IVACG Meeting, Arusha, Tanzania, March 1993. (International Nutrition Programme, University of Toronto, Canada). 10 mortality trials were recognised and 8 of these were used for a meta-analysis (complete data for Bombay and Haiti studies were not available). A summary estimate provided 23% reduction in mortality. A strong effect was demonstrable for diarrhoeal disease, an effect was demonstrable for measles (but n was very small); no effect could be established for respiratory disease. Results from 19 studies contributing information on morbidity effects were examined. There was a suggestion, consistent with the mortality results, that severe morbidity may be favourably influenced by vitamin A, but no evidence was found for any important effect on general morbidity incidence or prevalence.

Estimating the relative efficiency of a vitamin A intervention from population-based data. West K.P. Jr. et al. J Nep Med Assoc 1992; 30: 159-62 (Department of Ophthalmology, The Johns Hopkins School of Medicine, Baltimore, MD, USA). A simple, semi-quantitative technique is presented that identifies areas where programmes are likely to be relatively efficient in reaching areas with high xerophthalmia case-densities. An analysis based on data from a national blindness survey and the national census in 1981 indicated that a Terai-based effort would have a 7 to 34 times higher efficiency than programmes at higher elevations. (Ed. This kind of approach should assist those who have to make decisions about priorities for intervention. The validity of the basic data is, of course, crucial. In this case the Nepal Blindness Survey of 1981 was confined to winter months, December-April. Other data show that xerophthalmia may be highly seasonal, greater during the summer monsoon, but it is not known whether this applies equally everwhere. Throughout the whole country only 7204 children were examined with no case of corneal xerophthalmia found (the WHO prevalence level is 0.01%). Surveys of all causes of blindness at all ages where xerophthalmia is suspected should allow for adequate sample size of the at-risk age group and for seasonal

Tolerance of young infants to a single, large dose of vitamin A: A randomized community trial in Nepal. West K.P. Jr. et al Bull Wld Hlth Org 1992; 70: 733-9 (Dana Center for Preventive Ophthalmology, The Wilmer Eye Institute, Room 120, Baltimore MD 21287-9019, USA). Neonates received 50,000 IU vitamin A and infants 1-6 mo 100,000 IU or placebo (vitamin A group n=1461; controls n=1379). Neonates showed no excess risk of side-effects; older infants had 1.6% excess rate of vomiting and 0.5% excess rate of bulging fontanelles. There was no excess of loose stools, fever or irritability.

Vitamin A status of children in the urban slums of Karachi, Pakistan, assessed by clinical dietary and biochemical methods. Molla A. et al. Am J Trop Med Hyg 1993; 48: 89-96. (The Aga Khan University Medical Centre, PO Box 3500, Stadium Road, Karachi-74800, Pakistan). Random cluster sampling was made of 576 children (6-60 mo) in three slums. No definite clinical signs of xerophthalmia were observed. Serum retinol was deficient in 2% (less than 10 ug/dl); low in 46% (less than 20). Dietary vitamin A intake was assessed by the semiquantitative food frequency questionnaire of IVACG and had a mean value of 362 RE in the group with inadequate serum retinol and 431 in the adequate group. (Ed. The authors in their discussion raise an important problem of interpretation of serum retinol that is being seen in a number of studies now. By the WHO 1976 and 1982 criterion of 5% or more with less than 10 ug/dl there is not a public health problem here (2%); but by the criterion of PAHO 1970 of 15% or more with less than 20 ug/dl there is (48%). One cannot fault the conclusions of the authors — 'These results suggest that a significant number of children in these communities have low vitamin A levels and thus may constitute an at risk group'. I have several times urged for there to be a third Expert group convened by WHO for various reasons and this is another requiring urgent consideration).

Vitamin A status and lactation in Indonesian women. IVACG Meeting Arusha 1993. Stoltzfus R.J. et al (Division Nutrition Science, Cornell University, Ithaca, NY, USA). A single high dose of vitamin A given to the lactating mother improved the vitamin A status through 8 months postpartum.

Evaluation of a policy of routine high dose vitamin A therapy for children hospitalised with measles. IVACG Meeting, Arusha 1993. Hussey G. and Klein M. (Department of Pediatrics, University of Cape Town, South Africa). A retrospective study showed that high dose vitamin A (n=651) significantly reduced hospital stay, need for intensive care, and death compared with standard therapy (n=1061). Cost of vitamin A (US $0.33¢) resulted in saving of about $200.00 per case, excluding benedit of 64% reduction in

Appendix 11

INACG

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Appendix 12

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New from INACG

FRENCH AND SPANISH TRANSLATIONS OF ACTION PLAN ON IRON FORTIFICATION OF FOOD

For Immediate Release

Contact: Dr. Suzanne S. Harris
(202)-659-9024

Washington, D.C.-- Iron deficiency anemia is the most prevalent nutritional deficiency today, affecting more than 1 billion people worldwide. Iron fortification of food has proven successful in developed countries in combating iron deficiency anemia. French and Spanish translations of the latest INACG publication, *Combating Iron Deficiency Anemia Through Food Fortification Technology: An Action Plan*, provide direction for implementing national iron fortification programs in the developing world.

These publications present guidelines for implementors at the local, national, and international levels for conducting a country-specific iron fortification program. The *Action Plan* also shows how the partnerships between industry, donor agencies, and country leadership can build successful strategies for combating iron deficiency anemia.

This *Action Plan* represents the synthesis of ideas generated at the XII INACG Meeting, held 5-7 December 1990 in Washington, DC. The meeting brought together representatives from industry, academia, governments, and nonprofit organizations to discuss the theme "Combating Iron Deficiency Anemia Through Food Fortification Technology."

Single copies of the translations, entitled *Lutte contre l'anémie ferriprive par la technologie de fortification alimentaire: Un plan d'action*, and *Lucha contra la anemia por deficiencia de hierro mediante tecnología de fortificación de alimentos: Un plan de accion*, and other INACG publications are available free of charge to developing countries and for US$3.50 to developed countries. Order copies from the INACG Secretariat, The Nutrition Foundation, Inc., 1126 Sixteenth Street, NW, Washington, DC 20036, USA.

The International Nutritional Anemia Consultative Group was established in 1977 to guide international activities aimed at reducing iron deficiency anemia in the world.

21292

Single copies of this and other IVACG publications are available free of charge to representatives in developing countries and for US$3.50 to those in other nations. Order copies from the IVACG Secretariat, The Nutrition Foundation, Inc., 1126 Sixteenth Street, N.W., Washington, D.C. 20036, USA. Please make checks payable in U.S. dollars to The Nutrition Foundation.

Colleagues and organizations around the world contributed to the development of this resource book. The text reflects these contributions as well as the collective experiences of IVACG task force members and the critiques of several reviewers.

A cooperative agreement between the Office of Nutrition, Bureau for Research and Development, U.S. Agency for International Development and The Nutrition Foundation provided major support for this publication. The International Vitamin A Consultative Group was established in 1975 to guide international activities for reducing vitamin A deficiency in the world.

# # #

Appendix 13

INACG

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INTERNATIONAL NUTRITIONAL ANEMIA CONSULTATIVE GROUP

STEERING COMMITTEE MEETING

12 March 1993

Novotel Mt. Meru Hotel
Arusha, Tanzania

MINUTES

I. Call to Order

The meeting was called to order at 0907 by Dr. Samuel G. Kahn acting as the chairman in the absence of Dr. Richard Theuer. A list of those in attendance is attached. Dr. James Cook and Dr. Festo Kavishe joined the meeting as invited guests.

II. Approval of Minutes of the 6 November 1991 Steering Committee Meeting

Dr. Viteri moved to amend the INACG mission statement in the minutes to reorder the groups with which INACG works. The amended mission statement would read: "To facilitate the efforts of U.N. agencies, bilateral agencies, governments, private voluntary and nongovernmental organizations, and private industry to reduce nutritional anemia and its consequences by providing guidance and through an established international network of experts."

The amendment was accepted and the minutes approved as amended.

III. Secretariat Update on INACG Outreach Activities

- **Response to INACG Promotional Letter**

  Dr. Suzanne Harris reported that the secretariat now has over 120 names of individuals from 32 countries who have expressed interest in INACG. These will be made available to the steering committee. Dr. Harris reported that Dr. Viteri had offered to exchange the Group for the Control of Iron Deficiency (GCID) list of individuals interested in iron deficiency anemia with INACG to produce a combined directory.

- **Report on INACG Participation in Micronutrient Activities**

International Medical Services for Health (INMED) - Dr. Richard Theuer made a presentation on iron deficiency anemia at the Third Millennium conference sponsored by INMED in June 1992. INACG materials were distributed to the conference participants.

Program Against Micronutrient Malnutrition (PAMM) - At the request of Dr. Fritz van der Haar, Wageningen University, the secretariat arranged for a group of the PAMM trainees to visit a flour mill in Toledo, Ohio owned by the Nabisco Company. The group wanted to see the process of iron fortification of wheat flour. Unfortunately a snow storm prevented their visit.

The secretariat arranged for Dr. David Yeung, H.J. Heinz Company, to participate in the PAMM Industry Forum in December 1992.

Micronutrient Forum at the International Conference on Nutrition (ICN) - The secretariat arranged for Dr. George Purvis to address iron at the micronutrient forum sponsored Helen Keller International during the International Conference on Nutrition in Rome last December. He was well received and there was considerable interest from the audience on iron fortification.

Group for the Control of Iron Deficiency Anemia (GCID) of the Administrative Committee on Coordination-Subcommittee on Nutrition (ACC/SCN) - Dr. Viteri described GCID as a body formed to inform the SCN members about relevant activities and to promote support for iron deficiency control among the donor agencies. GCID sponsored a workshop with WHO and PAHO in Buenos Aires, Argentina in November 1992. The World Bank and IDRC (Canada) provided funding. Eight South American countries sent representatives along with an analysis of the prevalence of nutritional anemia and iron deficiency (NAID) in their country and an assessment of the resources available for controlling NAID. During the workshop the country representatives worked on national plans for controlling iron deficiency. As part of this plan they agreed to form a promotional group made up of representatives from industry, government, and others interested in NAID within three months.

Examples of some of the specific activities proposed in the country plans include production of fortified infant formula in Chile, Argentina, and Uruguay, and bread fortification in Ecuador. A summary of the workshop will be available in English. The Spanish text of the full meeting report is currently being reviewed. GCID is planning a second workshop in Caracas,

Venezuela and a third in Thailand.

Though GCID's role is not clearly defined, Dr. Viteri stated that the SCN created GCID to work with INACG. By working together GCID may be able to bring additional resources to INACG. Both the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) and the International Vitamin A Consultative Group (IVACG) took the initiative of establishing direct contact with the SCN.

Joint Micronutrient Consultative Group -- Dr. Kahn reported on the USAID-sponsored activities over the past year which involved representatives from all three micronutrient consultative groups -- ICCIDD, INACG, and IVACG. Together these representatives developed a coordinated approach to assessment of micronutrient status. A grid describing this coordinated assessment approach was provided in the meeting packets.

The group has also developed terms of reference for a pilot mission to the Philippines. The purpose of the mission is to determine the feasibility of coordinating efforts directed toward the three micronutrients and whether a mission approach to encouraging implementation of a coordinated effort is useful. Dr. Cook will be a member of the mission team.

Dr. Kavishe pointed out that Tanzania has a joint micronutrient program in place under the direction of the Tanzanian Food and Nutrition Center (TFNC). Through TFNC there is a national IVACG headed by the Department of Agriculture and a national INACG headed by the Department of Health. Each group has task forces devoted to supplementation and assessment which meet quarterly. These groups provide input to the national micronutrient plan.

For iron they have agreed on three strategies:

- increasing availability of vitamin C rich and dark green leafy vegetables;
- supplementation of pregnant women with iron and folate through the maternal and child health program; and
- parasite control in partnership with other government agencies.

The national INACG serves as a catalyst for planning and a conduit for interaction with the private sector including nongovernmental organizations. The World Bank is supporting the TFNC effort for 5 years. The mid-program review will be this year. Donor organizations serve as ex-officio members of the national consultative groups and therefore know what is happening. This helps to cement their commitment to the program.

While congratulating the Tanzanians on their success, several members of the steering committee pointed out that others had tried such ideas and failed. Dr. Kavishe and Dr. Maletnlema agreed that their success was due to the three independent consultative groups being coordinated by one group -- TFNC. Using a similar structure they have been successful in reducing protein calorie malnutrition by increasing food security.

TFNC is a part of the Ministry of Health and receives funding through the ministry. Parliament has enacted legislation authorizing the program. This helps to reduce the impact of changes in government leadership. The micronutrient strategic plan developed through the TFNC is incorporated in the ministry plans and reflected in the ministry budget requests.

IV. INACG Publications

- ***Combating Iron Deficiency Anemia Through Food Fortification Technology: An Action Plan***

  The secretariat reported that the Action Plan is available in English, French, and Spanish. Notices of its availability have been circulated to numerous newsletters and journals.

- **EDTA Monograph and Submission to the Joint FAO/WHO Expert Committee on Food Additives (JECFA)**

  The secretariat reported that the EDTA task force headed by Dr. Sean Lynch have completed the draft monograph. Following copy editing the monograph will be published.

  In addition to this activity, the secretariat hired Dr. Ian Munro, CanTox Inc., to develop a toxicology monograph and data sheet for review by JECFA at their February 1993 meeting. That review was successful in that JECFA provisionally agreed that Fe EDTA does not present a safety problem when used in supervised food fortification programs for iron deficient populations. Dr. Munro presented the Fe EDTA data to JEFCA and reported to the secretariat that the committee wanted better specification data for food grade material. The committee also suggested an additional animal study using doubly labeled Fe EDTA to see if any of the compound ends up in the animal's liver.

- **Revision Priorities**

  Following the last meeting the secretariat asked the steering committee to review the current INACG publications and suggest those requiring revision.

The group suggested the following: *Iron Deficiency in Infancy and Childhood, Measurements of Iron Status*, and *Iron Deficiency in Women.*

- **Social Marketing Paper**

The secretariat reviewed comments received from the Coca-Cola Company on the social marketing paper developed in 1987. The committee agreed that the proposal laid out in the paper was very ambitious and expensive. Clear delineation of benefits derived from reducing iron deficiency are needed. Dr. Cook described an video developed for promotion of beef consumption in New Zealand. The video effectively presents testimonials from athletes and students on the benefits of beef eating on physical and mental performance.

V. Discussion of Future Directions

The committee discussed a series of issues related to iron deficiency anemia. The points raised are summarized as follows.

- **Mental Development and Productivity**

The committee was not satisfied with the draft document circulated by the secretariat. Committee members indicated that the document needs to be updated in order to address treatment as well as prevention. Dr. Tomas Walter provided written comments to improve the scientific basis of the document.

Except for the recent paper by Ernesto Pollitt, all the studies show that anemic infants did not improve in measures of development upon refeeding with iron. Dr. Walter reported his findings after a 5 year follow-up of 70 children whose anemia was corrected. These children continue to show impaired IQ and school performance. Dr. Walter will check them again after 10 years.

In a new National Institutes of Health sponsored study, Dr. Walter and Dr. Lozoff, Case Western Reserve University, will try to determine if iron deficiency anemia or some other factor is responsible for the developmental impairment. A sample of 3600 infants who were exclusively breast fed from 0 to 6 months of life will be separated into two groups, one receiving iron fortified formula and the other receiving low iron formula from 6 to 12 months of age. These infants will be tested for iron deficiency anemia and developmental indicators. Some of the infants will be followed to 36 months of age. The mothers are all literate, but differences in home stimulation are still possible confounders.

During the discussion several points were raised in relation to the draft document. Dr. Maletnlema urged that the gravity of the problem be brought out, but asked for more work on methods as well. Hemoglobin is the most commonly collected indicator, but it is not specific for iron deficiency. It might be useful to pull together surveys that include serum ferritin values.

In Tanzania, maternal death linked to iron deficiency (hemoglobin values of 3-4) is an important problem. Dr. Viteri cautioned that the current systems might not be able to meet any new demands arising from successful advocacy activities. The full range of players need to be educated, not just the program planner. The technical people need to be well prepared first. INACG should not neglect other public health approaches such as parasite and malaria control that will also impact anemia prevalence.

- **Work Productivity**

This is an important topic given the increasing role of women in the work force.

- **Iron Overload**

This is an issue in Africa. Dr. Cook reported that Dr. Victor Herbert is very vocal about iron overload in the U.S. Dr. Viteri pointed to the need for targeted interventions to avoid the overload question. The International Life Sciences Institute is considering sponsoring a workshop on the issue of iron overload.

- **Iron Supplementation**

Several new strategies for improving compliance and efficacy of supplementation are being tried. The group agreed that supplementation should be targeted to pregnant women and women of reproductive age. Supplementation is not a long term cure and should not be left solely to the health community's jurisdiction. Dr. Cook reported the results of a slow release iron tablet (50 mg) trial in Jamaica. The single slow release tablet was as effective as two regular 60 mg tablets in raising hemoglobin levels.

Dr. Viteri reported preliminary findings in Chinese children given 6 mg iron/kg body weight weekly. Again the same rise in hemoglobin was seen when compared to daily dosing. A weekly dosing strategy would allow the tablets to be given during school rather than relying on compliance at home. Dr. Scrimshaw is planning to evaluate a weekly dose (60 mg) in women.

- **Fortification**

  Dr. Maletnlema stated that cost remains a major hurdle for national fortification programs in Africa. Products do not always reach the neediest populations. It may be important to organize fortification on a regional basis and involve industry through advisory groups.

- **Network Development Including Regional Coordination**

  There is a real need for regional collaboration. INACG could provide guidance directed to those responsible for national programs through a network of regional representatives. Such activities might draw in support from other multinational and bilateral organizations. Dr. Viteri offered to approach UNICEF once INACG has developed specific future activities.

VI. Strategies for the Coming Year

The committee asked the secretariat to develop a list of options based on the discussion and circulate them for comment to the committee. Based on the comments received the secretariat would develop a plan of action for INACG which would include components related helping with national planning and advocacy to reduce iron deficiency anemia.

The committee encouraged the secretariat to consider attaching the committee meetings to other related meetings including more general INACG meetings.

VII. Adjournment

As there was no further business, the meeting was adjourned at 1535.

Signed: Suzanne S. Harris

Suzanne S. Harris, Ph.D.
INACG Secretariat

Date: April 22, 1993

DRAFT INACG PLAN OF ACTION

Mission

To facilitate the efforts of U.N. agencies, bilateral agencies, governments, private voluntary and non-governmental organizations and private industry to reduce nutritional anemia and its consequences by providing guidance and know-how through an established international network of experts.

Proposed Activities

A. Advocacy Activities

1. Information, Education, and Communication

   Develop informational material on the link between nutritional anemia and human mental and motor development.

   Develop informational material on the detrimental effect of nutritional anemia on a population's capacity for economic development.

2. Network Development

   Approach other multinational and bilateral donors to join in INACG efforts.

   Expand contacts with interested experts in nutritional anemia worldwide.

B. Activities to Improve Intervention Strategies

1. Promote Iron EDTA as food fortificant

   Publish iron EDTA monograph.

   Promote use of iron EDTA by an appropriate country project or program.

   Develop more complete food grade specifications for iron EDTA.

2. Develop a comprehensive guide to strategies and options for national planning to combat nutritional anemia

C. Activities to Resolve Scientific Issues

1. Jointly sponsor with other interested organization a workshop to discuss the scientific issues surrounding questions of iron overload and develop recommendations appropriate to developing country situations.

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To facilitate the efforts of U.N. agencies, bilateral agencies, governments, private voluntary and non-governmental organizations and private industry to reduce nutritional anemia and its consequences by providing guidance and know-how through an established international network of experts.

Proposed Activities

A. Advocacy Activities

1. Information, Education, and Communication

Support the International Conference on Nutrition global strategy and action to combat iron deficiency anemia, as stated in the ICN Plan of Action for Nutrition, through the INACG's scientific, technical and programmatic experience in collaboration with international and national donors and operating agencies.

Develop informational material on the link between nutritional anemia and human development and performance including mental and motor development.

Develop informational material on the detrimental effect of nutritional anemia on a population's health and capacity for economic development.

Identify more effective methods of disseminating information on nutritional anemias, particularly among effected populations in developing countries.

Promote assessment and discernment of the problem of nutritional anemia at the national and international level.

2. Network Development

Approach other multinational and bilateral donors to join in INACG efforts.

Expand contacts with interested experts in nutritional anemia worldwide.

B. Activities to Improve Intervention Strategies

1. Promote Iron EDTA as food fortificant

   Publish iron EDTA monograph.

   Promote use of iron EDTA by an appropriate country project or program.

   Develop more complete food grade specifications for iron EDTA.

2. Promote studies on the use of local foods in combatting nutritional anemias.
3. Develop a comprehensive guide to strategies and options for national planning to combat nutritional anemia

C. Activities to Resolve Scientific Issues

1. Jointly sponsor with other interested organizations a workshop to discuss the scientific issues surrounding questions of iron overload as an issue to be considered in different settings and develop recommendations appropriate to developing country situations.

2. Jointly sponsor with other international organizations a workshop to discuss the scientific issues of hemoglobin levels as a function of race, sex, and age.

October 1993

Appendix 14

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Appendix 15

Iron EDTA for Food Fortification

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UNIQUE COMPOUND TO COMBAT IRON DEFICIENCY ANEMIA: MOST COMMON NUTRITIONAL DEFICIENCY

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Washington, D.C. -- The International Nutritional Anemia Consultative Group (INACG) has just released a new publication on a novel iron compound that will help developing countries combat iron deficiency anemia, the world's most common nutritional deficiency, affecting one out of every six people. The new monograph, entitled *Iron EDTA for Food Fortification*, was produced by INACG with the support and encouragement of the U.S. Agency for International Development (USAID), which has for many years been a leader in addressing the problem of iron deficiency anemia.

People in developing countries now stand to benefit from an exciting iron fortification compound that can be easily added to their diets. A compound called iron EDTA (sodium iron ethylenediaminetetraacetic acid) was provisionally approved this year by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) for food fortification programs and is the subject of a just-released publication designed to help developing countries use it.

Iron EDTA for Food Fortification provides governments, industry, donor agencies, nongovernmental organizations, and research institutions with the scientific and technical information on the safety and efficacy needed to establish iron EDTA food fortification programs. It was prepared by a distinguished group of experts under the auspices of INACG.

Iron EDTA "represents a major addition to the iron arsenal because this unique iron compound can be used in diets where conventional food iron compounds cannot--high cereal or legume diets," said Richard Seifman, director of the Office of Nutrition at USAID. Iron EDTA makes iron available for absorption from cereals and legumes, which form the basis of diets in many developing countries. It does so without altering the taste, smell,

154

altering the taste, smell, or color of the fortified foods. (For many years USAID has been involved in supporting and encouraging interest in iron EDTA.)

Widespread fortification of cereals and legumes with iron EDTA could greatly reduce iron deficiency during early childhood, thus preventing permanent impairment of mental and motor development. Also standing to benefit are pregnant women. These vulnerable groups are particularly prone to iron deficiency anemia and its consequences, such as greater risk of infection, premature delivery, increased maternal deaths, and low birth-weight babies. Not to mention the adverse effects on school achievement and worker productivity.

The economic and social impact of this preventable condition is enormous. Substantially reducing iron deficiency in women and children by the year 2000 is a goal adopted at the World Summit for Children in 1990, and the 1992 International Conference on Nutrition.

Iron EDTA can make a difference.

Single copies of *Iron EDTA for Food Fortification* are available free of charge to appropriate developing country professionals, and for US$3.50 for those in developed countries. Copies can be obtained from the INACG Secretariat, The Nutrition Foundation, Inc. 1126 Sixteenth Street, NW, Washington, D.C. 20036, USA. Make checks payable (in US dollars only please) to INACG.

The International Nutritional Anemia Consultative Group was established in 1977 to guide international activities aimed at reducing iron deficiency anemia in the world. INACG receives support through a cooperative agreement between The Nutrition Foundation, Inc. and the Office of Nutrition, Bureau for Research and Development, U.S. Agency for International Development.

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Appendix 16

SODIUM IRON EDTA

1. EXPLANATION

Sodium iron EDTA (NaFeEDTA) has not previously been evaluated by the Joint FAO/WHO Expert Committee on Food Additives. However, disodium and calcium disodium EDTA were evaluated and a monograph was published in WHO Food Additive Series 5 (JECFA, 1974). The ADI based on $CaNa_2EDTA$ was established as 2.5 mg EDTA/kg body weight/day.

Data is presented herein which supports the contention that this ADI is also applicable to NaFeEDTA. The monograph has been updated, and relevant sections are reproduced below.

With respect to iron, a provisional maximum tolerable daily intake of 0.8 mg/kg/day was established by the Committee in the twenty-seventh report (JECFA, 1983). The view stated at the twenty-sixth meeting, that the tolerable daily intake should not be used as a guide for fortifying processed foods, was reiterated. No new information relating to iron toxicology is presented in this monograph.

It has been estimated that 500-600 million of the world's 5 billion inhabitants suffer from nutritional iron deficiency anaemia (MacPhail and Bothwell, 1992). Most of these individuals live in developing countries where the prevalence of iron deficiency anaemia may be as high as 60-70% in preschool children and 60-80% in pregnant women (Bothwell et al., 1979; Simmons and Gurney, 1980).

The physiologic and economic consequences of iron deficiency occur at all ages, although the most significant effect on the individual may vary depending on his or her stage of development. From the public health point of view, iron deficiency places a severe handicap on the productivity of society owing to the long term consequences of premature birth, impaired cognitive achievement and reduced ability to carry out physically demanding tasks.

Iron fortification of the diet is the only cost effective long term strategy for reducing the prevalence of iron deficiency in most developing countries (Cook and Reusser, 1983; MacPhail and Bothwell, 1992). A proposed strategy for iron fortification in developing countries involves the use of NaFeEDTA. Despite the continuing high prevalence of iron deficiency in many developing countries and 40 years of research, iron fortification is not practised in developing countries. There are many reasons why this is so, but one of the most important is the practical difficulty of adding bioavailable iron to food in a form that will ensure its absorption. It is against this background that NaFeEDTA merits further consideration. It has as not yet been used because there has been some concern about the safety of prolonged ingestion of EDTA owing to the possibility of interactions with other trace metals. Data supporting the safety of NaFeEDTA as a food fortificant in developing countries are presented in this monograph.

2. BIOLOGICAL DATA

2.1 Biochemical aspects

The biochemistry of EDTA metal complexes is inextricably tied to their chemical properties. An understanding of these chemical properties is essential in interpreting the biochemistry and toxicology of EDTA metal complexes. A brief discussion of the chemical properties of EDTA metal complexes is presented here to facilitate understanding of the material that follows.

Ethylenediaminetetraacetic acid (EDTA) is a hexadentate chelator capable of combining stoichiometrically with virtually every metal in the periodic table (Chaberck and Martell, 1959). With divalent or trivalent metal ions a neutral or anionic metal chelate results. The metal is largely prevented from reacting with competing anions and its solubility is greatly increased. The effectiveness of EDTA as a chelate for a particular metal ion is given by its stability constant with the metal ion. Chelation potential is affected by pH, the molar ratio of chelate to metal ion, and the presence of competing metal ions capable of forming complexes with EDTA (Plumb et al., 1950; Martel, 1960; Hart, 1984). The stability constants for different metal-EDTA complexes vary considerably and any metal which is capable of forming a strong complex with EDTA will at least partially displace another metal.

Of the nutritionally important metals, Fe^{3+} has the highest stability constant (log k of 25.1), followed by Cu^{2+} with 18.4, Zn^{2+} with 16.1, Fe^{2+} with 14.6, Ca^{2+} with 10.6, Mg^{2+} with 8.7 and Na^{+} with 1.7 (West and Sykes, 1960). The situation is somewhat complicated by each metal having an optimum pH for chelate formation ranging from pH 1 for Fe^{3+}, to pH 3 for Cu^{2+}, pH 4 for Zn^{2+}, pH 5 for Fe^{2+}, pH 7.5 for Ca^{2+}, and pH 10 for Mg^{2+} (West and Sykes, 1960). When NaFeEDTA is ingested with foods, the Fe^{3+} ion would be expected to remain firmly bound to the EDTA moiety during passage through the gastric juice, but could be exchanged for Cu^{2+}, Zn^{2+}, Fe^{2+} or Ca^{2+} in the duodenum. Similarly when Na_2EDTA and $Na_2CaEDTA$ are consumed with foods, the Na^{+} and Ca^{2+} ions would be predominantly exchanged in the gastric juice for Fe^{3+} ions, which could again in turn be exchanged for Cu^{2+}, Zn^{2+}, Fe^{2+} or Ca^{2+} further down the gastrointestinal tract. The extent to which the metal EDTA complexes form is dependent on the pH and the concentration of the competing metals as well as competing ligands. The lower stability constant and higher pH optimum of the Mg-EDTA chelate make reaction with this metal less likely.

An appreciation of the chelating properties of EDTA with respect to iron provide the basis of our understanding of the observed effects of EDTA on food iron absorption. Ferric food iron is poorly absorbed by human beings because it is precipitated from solution above pH 3.5 unless suitable complexing agents are present. It may therefore be partially insoluble in the upper small intestine where most nonhaem iron is absorbed (Conrad and Schade, 1968; MacPhail et al., 1981). When EDTA is present in a meal, iron (primarily Fe^{3+}) remains complexed with EDTA under the acidic conditions prevailing in the stomach. The chelate holds the iron in solution as the pH rises in the upper small intestine, but the strength of the complex is progressively reduced allowing at least partial exchange with other metals and the release of some of the iron for absorption. There is convincing evidence that iron chelated by EDTA (NaFeEDTA) is available for absorption via the physiologically regulated pathways responsible for iron uptake (Candela et al., 1984). The results of absorption studies with NaFeEDTA

indicate that iron is dissociated from the EDTA moiety prior to absorption. The results of these studies are summarized in Section 2.1.1.

2.1.1 Absorption, distribution and excretion

Absorption and excretion of Fe from NaFeEDTA - injection studies

When NaFeEDTA is injected intravenously into rats most of the iron (70% - 90%) is lost through the urine within 24 hours (Najarajan et al., 1964; Anghileri, 1967). A small proportion enters the physiological iron pool destined primarily for haemoglobin synthesis probably because of the slow release of iron to the iron transport protein, transferrin, in the circulation (Bates et al., 1967). After intramuscular or intraperitoneal injection a greater proportion of the iron is available for physiological exchange with compartments in the bone marrow and liver. The longer contact time between transferrin and EDTA, allows for greater transfer of iron from the chelate to the physiological transport protein (Rubin et al., 1970).

FeEDTA administered intravenously to humans was almost quantitatively excreted in urine (Lapinleimu and Wegelius, 1959).

Absorption and excretion of Fe from NaFeEDTA - oral studies

Human iron deficiency anaemia was successfully treated with FeEDTA given orally with 84% of labelled FeEDTA excreted in the faeces and none in the urine. Red cells, however, contained labelled Fe and reticulocytosis occurred (Will and Vilter, 1954).

Studies carried out in swine using a dual labelled $Na^{55}Fe[2\text{-}^{14}C]EDTA$ preparation demonstrated rapid transfer of ^{55}Fe to the plasma with a peak at 1 hour and subsequent incorporation of 4.6% of the administered dose into circulating haemoglobin (Candela et al., 1984). A small fraction (0.3%) of the ^{55}Fe administered was excreted in the urine. In contrast to the ^{55}Fe only a small percentage of the ^{14}C could be detected in the plasma at any time. Absorption occurred over an extended period (5-20 hours). A total of about 5% of the ^{14}C labelled EDTA was eventually absorbed in the duodenum and jejunum and quantitatively excreted in the urine.

In a parallel experiment when 5 mg Fe as $Na^{59}FeEDTA$ was given to six fasting human volunteers, mean radioiron absorption as measured by red blood cell utilization was 12.0% (Candela et al., 1984). Only 0.3% of the administered dose of iron was excreted in the urine. The studies demonstrate that Fe and EDTA are absorbed independently when NaFeEDTA is administered by mouth.

Similar conclusions were reached in an earlier human absorption study carried out by MacPhail et al. (1981). $Na^{59}FeEDTA$ was administered to human volunteers. Between 3 and 25% of the ^{59}Fe was absorbed, but less than 1% of the administered ^{59}Fe appeared in the urine over the subsequent 24 hours. All ^{59}Fe absorbed in the form of the intact $Na^{59}FeEDTA$ complex would be expected to be excreted in the urine within 24 hours (based on the results of Najarajan et al., 1964 and Anghileri, 1967) demonstrating again that most of the iron is released from the EDTA complex before absorption. Similar conclusions have been reached with another iron

chelator (nitrilotriacetic acid), the properties of which have been studied extensively in experimental animals (Simpson and Peters, 1984).

Absorption and excretion of EDTA from EDTA metal chelates

Rat:

^{14}C-labelled $CaNa_2EDTA$, when fed to rats in doses of 50 mg/kg bw, was absorbed only to an extent of 2 to 4%; 80 to 90% of the dose appeared in the faeces within 24 hours, and absorption was still apparent at 48 hours. At the low pH of the stomach the calcium chelate is dissociated with subsequent precipitation of the free acid (EDTA), and this is only slowly redissolved in the intestine (Foreman et al., 1953).

In feeding experiments, in rats receiving disodium EDTA at dietary levels of 0.5, 1.0 and 5.0%, the faeces contained 99.4, 98.2 and 97.5% of the excreted material (Yang, 1964).

Similar experiments conducted also in rats gave essentially the same results. Thirty-two hours after a single dose of 95 mg disodium EDTA/rat, 93% was recovered from the colon. After doses of 47.5, 95.0 and 142.5 mg disodium EDTA the amount of EDTA recovered in the urine was directly proportional to the dose given, suggesting that EDTA was absorbed from the gastrointestinal tract by passive diffusion. The motility of the intestine was not affected by the compound (Chan, 1964).

When 200 mg $CaNa_2EDTA$ was introduced into the duodenum of rats an absorption rate of 6.5 to 26% was observed (Srbrova and Teisinger, 1957).

The maximum radioactivity in the urine after application of ^{14}C-labelled $CaNa_2EDTA$ to the skin was only 10 ppm (0.001%) (Foreman and Trujillo, 1954).

Human:

Experiments in man also revealed poor absorption; only 2.5% of a 3 g dose given was excreted in the urine (Srbrova and Teisinger, 1957). These authors also confirmed the dissociation of the calcium chelate in the stomach. A dose of 1.5 mg of ^{14}C-labelled $CaNa_2EDTA$ given in a gelatine capsule to normal healthy men was absorbed to an extent of 5% (Foreman et al., 1954).

The absorption of the EDTA moiety from orally administered NaFeEDTA has not been measured directly in humans. However physicochemical considerations indicate that EDTA absorption from NaFeEDTA would be similar to that from other metal complexes, such as $CaNa_2EDTA$ and CrEDTA. As described above, poor absorption of the intact NaFeEDTA can be inferred from the measurements of urinary radioiron excretion after the oral administration of $Na^{59}FeEDTA$ made by MacPhail and coworkers (1981).

Similar results have been obtained with a tightly bound chelate, ^{51}CrEDTA from which any released metal is very poorly absorbed (Bjarnason et al., 1983; Aabakken and Osnes, 1990). Only 1-5% of a dose of ^{51}CrEDTA given in a fasting state is absorbed by the healthy intestinal

mucosa. In the presence of disorders of the gastrointestinal tract the absorption may be doubled. The ^{51}CrEDTA that is absorbed appears to be taken up through intercellular junctions as the intact complex. The amount absorbed has been used as a measure of the integrity of the bowel mucosa.

In summary, most of the iron in NaFeEDTA is released to the physiological mucosal uptake system before absorption. Only a very small fraction of the NaFeEDTA complex (less than 1%) is absorbed intact and this is completely excreted in the urine. An additional small fraction (less than 5%) of the EDTA moiety is absorbed, presumably bound to other metals in the gastrointestinal tract, and is also completely eliminated in the urine.

Bioavailability of iron from NaFeEDTA

The results of iron absorption studies comparing the bioavailability of iron from $FeSO_4$ and NaFeEDTA fortified foods are listed in Table 1. For purposes of comparison the individual absorption values have been standardized to a reference absorption of 40% to remove the influence of varying iron requirements in different subjects. A reference absorption value of 40% is assumed to represent borderline iron deficiency (Hallberg et al., 1978). The bioavailability of iron from $FeSO_4$ varies over a wide range and correlates with the relative proportions of enhancers and inhibitors known to be present in the meals. In contrast, the absorption of iron from NaFeEDTA eaten with identical meals varies only two to three fold. More iron was absorbed from the meals containing NaFeEDTA in all but one case in which Na_2EDTA and $FeSO_4$ were eaten with sugar cane syrup (see Table 1). Enhanced bioavailability was most marked in meals with poor $FeSO_4$ bioavailability ($FeSO_4$ absorptions less than 4%). Between 2.1 to 2.9 times as much iron was absorbed under such circumstances. This point is exemplified by the results of the study by Viteri *et al.* (1978) (see Table 1) in which iron absorption from a NaFeEDTA-fortified meal of beans, maize, and coffee was 2.7 times greater than that from the same meal containing $FeSO_4$ (Viteri et al., 1978).

The absorption of Fe from NaFeEDTA has been studied in a wide variety of meals. Comparisons with iron absorption from simple iron salts have not always been made. However, some studies provide useful information about the suitability of three staple food items as potential vehicles for fortification with NaFeEDTA. This information is summarized in Table 2. Some studies listed in Table 1 have been included under the appropriate categories (all values are corrected to 40% reference absorption, or a serum ferritin of 27 μg/l). It is evident that approximately 10% of the fortification iron added would be absorbed by iron deficient individuals if these staple foods were used as the vehicle for delivering the fortificant.

Effect of NaFeEDTA on bioavailability of Intrinsic Food Iron

Conclusions drawn from much of the experimental work on food iron absorption and iron fortification are based on the observation that soluble iron added to a meal and the intrinsic nonhaem food iron behave as a common pool, which is equally susceptible to enhancers and inhibitors of iron absorption present in the meal (Cook et al., 1972; Hallberg and Bjorn-Rasmussen, 1972); NaFeEDTA shares this property. When Na^{59}FeEDTA was added to meals containing foods labelled intrinsically with ^{55}Fe, the ratio between the proportions of iron absorbed from the two sources was close to unity (Layrisse and Martinez-Torres, 1977; Matrinez-Torres et al., 1979; MacPhail et al., 1981), with the exception of one study in which

$Na^{59}FeEDTA$ fortified sugar was sprinkled onto ^{55}Fe-labelled maize immediately before it was eaten (MacPhail et al., 1981). These results indicate that the $Na^{59}FeEDTA$ equilibrates with the common pool, since without such equilibration, the amount of food iron absorbed would be much lower than the amount absorbed from NaFeEDTA (MacPhail et al., 1981). Inadequate mixing of the NaFeEDTA-fortified sugar with the maize meal probably accounted for the lack of equilibration in the one inconsistent study reported by MacPhail et al. (1981). These results reveal another important property of NaFeEDTA. Equilibration of NaFeEDTA with the common pool iron improves the bioavailability of the intrinsic food iron as well. Therefore NaFeEDTA improves iron balance by supplying iron in a form less affected by dietary inhibitors, but also improves the absorption of nonhaem iron in the meal derived from other sources.

This point is further illustrated by the results of a number of studies which demonstrate that the positive effects of EDTA on iron absorption are shared by other elements of the common pool, such as another iron salt added to the meal. When $FeSO_4$ and NaFeEDTA were fed to humans on separate days in the same type of meal (maize porridge), iron absorption from the NaFeEDTA fortified meal was significantly better. However the iron from $FeSO_4$ was as well absorbed as that from NaFeEDTA when they were fed together in the same meal (MacPhail et al., 1981; Martinez-Torres et al., 1979). More direct evidence of reciprocal exchange between food iron and iron added as NaFeEDTA was provided by experiments in which subjects were given maize porridge fortified with equimolar quantities of $^{59}FeSO_4$ and $Na^{55}FeEDTA$ (McPhail et al., 1981). The ratio between the two isotopes was almost the same in the meal and the urine. This implies that exchange of iron between $FeSO_4$ and NaFeEDTA must occur before absorption of the chelate, since only the small amount of iron (less than 1%) absorbed as the intact chelate would subsequently appear in the urine (for explanation see section 2.1).

The effect of Na_2EDTA on iron absorption

Na_2EDTA is widely used as a food additive to prevent oxidative damage by free metals. Since Na_2EDTA readily chelates iron in the gut to form NaFeEDTA, its effect on iron absorption is of interest. In a recent study (el Guindi et al., 1988) Na_2EDTA was added, together with an equimolar quantity of iron as $FeSO_4$, to bread with a high concentration of phytate (an inhibitor of iron absorption). The combination was associated with a 2.6x enhancement in iron absorption when compared with results with $FeSO_4$ used alone. Mean percentage iron absorption was approximately equivalent to that reported in other similar studies using NaFeEDTA. It is evident that the same effect on iron absorption can be achieved in meals containing compounds that inhibit iron absorption by adding Na_2EDTA and a soluble iron salt as is the case for adding NaFeEDTA.

The effects of Na_2EDTA on iron absorption appear to be influenced by the molar ratio of EDTA to iron. Earlier work suggested that increasing the molar ratio of Na_2EDTA to Fe was associated with a progressive reduction in iron absorption (Cook and Monsen, 1976). These observations have been extended recently (MacPhail and Bothwell, unpublished data, 1992). Iron absorption from a series of rice meals containing Na_2EDTA and iron in a molar ratio of 1:1 was compared to rice containing Na_2EDTA and iron in molar ratios (EDTA:Fe) ranging from 0:1 to 4:1. Statistically significant enhancement of absorption occurred at ratios of Fe:EDTA between 1:4 and 1:1. The enhancing effect of EDTA on iron absorption appeared to be maximal at a molar ratio (EDTA:Fe) of approximately 1:2, not 1:1 as previously assumed. At this molar

ratio over three times as much iron was absorbed from the EDTA containing meal as was the case for the control meal containing no EDTA.

Distribution

After parenteral administration to rats, 95 to 98% of injected ^{14}C-labelled $CaNa_2EDTA$ appeared in the urine within six hours. All the material passed through the body unchanged. Peak plasma levels were found approximately 50 minutes after administration. Less than 0.1% of the material was oxidized to $^{14}CO_2$, and no organs concentrated the substance. After i.v. injection, $CaNa_2EDTA$ passed rapidly out of the vascular systems to mix with approximately 90% of the body water, but did not pass into the red blood cells and was cleared through the kidney by tubular excretion as well as glomerular filtration (Foreman et al., 1953). The same was also found in man using ^{14}C-labelled $CaNa_2EDTA$. Three thousand milligrams were given i.v. to two subjects and were almost entirely excreted within 12 to 16 hours (Srbrova and Teisinger, 1957). These results indicate that intact $CaNa_2EDTA$, and presumably other EDTA metal complexes are rapidly excreted and do not accumulate.

2.1.2 Biotransformation

Neither the iron or EDTA moiety of NaFeEDTA undergoes biotransformation. Evidence for this conclusion comes from studies discussed in the previous section which indicated that both EDTA and iron are excreted unchanged following ingestion of NaFeEDTA.

2.1.3 Influence of EDTA compounds on the biochemistry of metals

EDTA removes about 1.4% of the total iron from ferritin at pH 7.4 to form an iron chelate (Westerfeld, 1961). Transfer of Fe from Fe-transferrin to EDTA in vitro occurs at a rate of less than 1% in 24 hours. In vivo studies in rabbits demonstrated transfer of iron only from FeEDTA to transferrin and not the reverse. It appeared that tissue iron became available to chelating agents including EDTA only when an excess of iron was present (Cleton et al., 1963). Equal distribution between a mixture of EDTA and siderophilin was obtained only at EDTA:siderophilin ratios of 20-25:1 (Rubin, 1961).

Addition of 1% Na_2EDTA to a diet containing more than optimal amounts of iron and calcium lowered the absorption and storage or iron in rats and increased the amount present in plasma and urine. The metabolism of calcium, however, was apparently unaffected (Larsen et al., 1960). A diet containing 0.15 mg of iron, 4.26 of calcium and 1 mg of EDTA per rat (equivalent to 100 ppm (0.01%) in the diet) for 83 days had no influence on calcium and iron metabolism, e.g. the iron content of liver and plasma (Hawkins et al., 1962).

Cu absorption and retention were improved at 500 mg EDTA/kg but not at 200 mg or 1000 mg EDTA/kg (Hurrell et al., 1992). Apart from a very small increase in urinary Cu excretion, dietary EDTA had no influence on Cu metabolism.

$CaNa_2EDTA$ increased the excretion of zinc (Perry and Perry, 1959), and was active in increasing the availability of zinc in soybean containing diets to poults (Kratzer et al., 1959). $CaNa_2EDTA$ enhanced the excretion of Co, Hg, Mn, Ni, Pb, Ti and W (Foreman, 1961). The

treatment of heavy metal poisoning with $CaNa_2EDTA$ has become so well established that its use for more commonly seen metal poisonings, e.g. lead, is no longer reported in the literature (Foreman, 1961). EDTA could not prevent the accumulation of ^{90}Sr, ^{106}Ru, ^{141}Ba and ^{226}Ra in the skeleton. ^{91}Y , ^{239}Pu and ^{238}U responded fairly well to EDTA, the excretion being accelerated (Catsch, 1961).

Food fortification with NaFeEDTA may be expected to increase Zn and Cu absorption and retention but not Ca or Mg. A diet containing RDA quantities of each metal (800 mg Ca and, 350 Mg, 10 mg Zn, and 2 mg Cu) which was fortified with 10 mg Fe as NaFeEDTA would contain a 1.5 molar excess of EDTA over Zn, an 8-fold molar excess of EDTA over Cu, but 80 times less EDTA than Ca and 50 times less EDTA than Mg on a molar basis. The small quantity of chelate with respect to Ca and Mg would be unlikely to have any detrimental effect. Both NaFeEDTA and NaEDTA may increase the absorption and retention of Zn and Cu when added to low bioavailability diets. This conclusion is supported by experiments with turkey poults (Kratzer et al., 1959), chicks (Scott and Ziegler, 1963) and rats (Forbes, 1961) which have demonstrated that Zn bioavailability and animal growth is improved when Na_2EDTA is added at 150-300 mg/kg to animal rations based on soybean protein isolate. The enhancing effect of EDTA on zinc absorption in these studies can be explained by a combination of two factors. Firstly, EDTA forms soluble chelates with Zn from which the metal is potentially absorbable, and secondly, Zn is prevented from forming non-absorbable complexes with phytic acid. EDTA does not enhance Zn absorption when absorption inhibitors are absent from the meal as evidenced by the observation that Na_2EDTA (1000 mg/kg) improved Zn absorption in rats fed a casein-based diet with added phytic acid, but had no effect in the absence of phytic acid (Oberleas et al., 1966). Other chelating substances can also enhance Zn absorption from low bioavailability diets. Vohra and Kratzer (1964) compared the growth promoting effect of chelates with stability constants (log k) for Zn varying from 5.3 to 18.8 in turkey poults fed zinc deficient diets based on soy protein isolate. They found that ethylenediaminediacetic acid-dipropionic acid, hydroxyethyl-EDTA, and EDTA (stability constants 14.5, 14.5 and 16.1, respectively) were the most effective.

These earlier observations were made with Na_2EDTA. However, NaFeEDTA has been shown to have similar properties in a recent study (Hurrell et al., 1992). Zinc, copper and calcium balances were performed in rats fed low Zn (6.1 mg/kg) soybean based diets containing 36 mg/kg added Fe as either ferrous sulphate or NaFeEDTA. In some experimental groups additional Na_2EDTA was added to the diet containing NaFeEDTA to give dietary EDTA levels of 200, 500 and 1000 mg/kg. Changing the iron compound in the diet from ferrous sulphate to NaFeEDTA at a level of 200 mg/kg increased apparent Zn absorption, urinary Zn excretion and Zn retention significantly ($p < 0.05$), but caused no changes in Cu or Ca absorption or excretion. Increasing the dietary EDTA level to 500 mg/kg (molar ratio EDTA:Zn, 19:1) and 1000 mg/kg (molar ratio EDTA:Zn, 38:1) further increased both Zn absorption and urinary Zn excretion. At the highest dietary EDTA level (1000 mg/kg), Zn retention was significantly higher than with no dietary EDTA, but lower than with 500 mg/kg EDTA. This resulted from an increase in urinary excretion of Zn to 15.6% of intake. Similar results were obtained with a Zn-sufficient (30 mg/kg) soybean diets, but more EDTA was required to achieve optimal ratios for improved absorption.

The studies of Hurrell et al. (1992) demonstrate that an 11-fold molar excess of EDTA over Cu increased Cu absorption and retention but that neither a 4.5 nor 23-fold molar excess had a significant effect. A human diet containing the RDA for Zn and Cu which was fortified with 10 mg Fe as NaFeEDTA would be expected to contain a 1.5 molar excess of EDTA over Zn and an 8-fold molar excess of EDTA over Cu. NaFeEDTA fortification would therefore be expected to have very little effect on Zn and Cu balance. A small beneficial effect could occur in meals containing little Zn or Cu or large quantities of phytate.

The applicability of the observations made in experimental animals to human nutrition has been confirmed by recent observations made by Hurrell's group (Davidsson, Kastenmayer and Hurrell, unpublished data, 1992). The metabolism of Zn and Ca was studied using a stable isotope technique in 10 adult women fed a breakfast meal of bread rolls made from 100 g high extraction wheat flour and fortified with 5 mg Fe as $FeSO_4$ or NaFeEDTA. The test meals contained a 3.3 molar excess of EDTA over Zn but some 10-fold less EDTA than Ca. Changing the Fe fortification compound from ferrous sulphate to NaFeEDTA significantly increased ^{70}Zn absorption ($p < 0.05$) from this meal from 20.9% to 33.5%. Urinary ^{70}Zn excretion also rose from 0.3% to 0.9%. Calcium metabolism was similar with the two different iron compounds. Earlier studies using less precise methodology have led to similar conclusions. Solomons et al. (1979) reported that adding NaFeEDTA to a low bioavailability Guatemalan meal did not influence Zn absorption by human subjects. However, as these workers measured Zn absorption based on plasma Zn concentrations after ingesting 25 mg Zn with a meal, the molar concentration of EDTA was some 10-fold less than that of Zn and an improvement in Zn absorption would not be expected. Finally no significant changes in plasma Zn concentration were observed in field studies in which NaFeEDTA was used as a food fortificant over a two year period (Viteri et al., 1983, Ballot et al., 1989b).

2.1.4 Effects on enzymes and other biochemical parameters

EDTA had a lowering effect on serum cholesterol level when given orally or i.v. It may have acted by decreasing the capacity of serum to transport cholesterol (Gould, 1961). Disodium EDTA had a pyridoxin-like effect on the tryptophan metabolism of patients with porphyria or scleroderma, due to a partial correction of imbalance of polyvalent cations (Lelievre and Betz, 1961).

In vitro, 0.0033 M EDTA inhibited the respiration of liver homogenates and of isolated mitochondria of liver and kidney (Lelievre and Betz, 1961). The acetylation of sulphanilamide by a liver extract was also inhibited (Lelievre, 1960). EDTA stimulated glucuronide synthesis in rat liver, kidney and intestines but inhibited the process in guinea-pig liver (Pogell and Leloir, 1961; Miettinen and Leskinen, 1962). Of the heavy metal-containing enzymes, EDTA at a concentration of about 10^{-3} M inhibited aldehyde oxidase and homogentisinase. Succinic dehydrogenase, xanthine oxidase, NADH-cytochrome reductase and ceruloplasmin (oxidation of p-phenylenediamine) were not inhibited (Westerfeld, 1961). Disodium EDTA was found to be a strong inhibitor for δ-aminolevulinic acid dehydrogenase, 5.5×10^{-6} M causing 50% inhibition (Gibson et al., 1955). The i.p. injection of 4.2 mmol/kg bw (equivalent to 1722 mg/kg bw) $CaNa_2EDTA$ caused in rats an inhibition of the alkaline phosphatase of liver, prostate and serum up to four days depending on the dose administered; zinc restored the activity (Nigrovic, 1964).

In vitro, EDTA inhibited blood coagulation by chelating Ca. The complete coagulation inhibition of human blood required 0.65-1.0 mg/ml. The i.v. injection of 79-200 mg EDTA/rabbit had no effect on blood coagulation (Dyckerhoff et al., 1942).

I.v. injections of Na_2EDTA and $CaNa_2EDTA$ had some pharmacological effect on the blood pressure of cats; 0-20 mg/kg bw $CaNa_2EDTA$ (as Ca) produce a slight rise; 20-50 mg/kg, a biphasic response; and 50 mg/kg, a clear depression (Marquardt and Schumacher, 1957).

One per cent Na_2EDTA enhances the absorption of ^{14}C-labelled acidic, neutral and basic compounds (mannitol, inulin, decamethenium, sulphanilic acid and EDTA itself) from isolated segments of rat intestine, probably due to an increased permeability of the intestinal wall (Schanker and Johnson, 1961).

2.2 Toxicology studies

2.2.1 Acute toxicity studies

(a) Disodium EDTA

Animal	Route	LD_{50} (mg/kg bw)	References
Rat	oral	2 000 - 2 200	Yang, 1964
Rabbit	oral	2 300	Shibata, 1956
	i.v.	47[a]	Shibata, 1956

[a]Dose depending on the rate of infusion

(b) Ca-disodium EDTA

Animal	Route	LD_{50} (mg/kg bw)	References
Rat	oral	10 000 $\pm$ 740	Oser et al., 1963
Rabbit	oral	7 000 approx.	Oser et al., 1963
	i.p.	500 approx.	Bauer et al., 1952
Dog	oral	12 000 approx.	Oser et al., 1963

The oral LD_{50} in rats is not affected by the presence of food in the stomach or by pre-existing deficiency in Ca, Fe, Cu or Mn (Oser et al., 1963).

Oral doses of over 250 mg/animal cause diarrhoea in rats (Foreman et al., 1953).

There are many reports in the literature on kidney damage by parenteral over-dosage of CaEDTA. A review was given by Lechnit (1961). Lesions simulating "versene nephrosis" in man have also been produced in rats. Disodium EDTA in doses of 400-500 mg i.p. for 21 days caused severe hydropic degeneration of the proximal convoluted tubules of the kidneys. $CaNa_2EDTA$ produced only minimal focal hydropic changes in 58% of animals, disappearing almost two weeks after stopping the injections (Reuber and Schmieller, 1962).

2.2.2 Short-term studies

Rat:

Groups of five male rats received 250 or 500 mg/kg bw $CaNa_2EDTA$ i.p. daily for three to 21 days and some were observed for an additional two weeks. Weight gain was satisfactory and histology of lung, thymus, kidney, liver, spleen, adrenal, small gut and heart was normal except for mild to moderate renal hydropic change with focal subcapsular swelling and proliferation in glomerular loops at the 500 mg level. There was very slight involvement with complete recovery at the 250 mg level. Lesions were not more severe with simultaneous cortisone administration (Reuber and Schmieller, 1962).

Groups of three male and three female rats were fed for four months on a low mineral diet containing one-half the usual portion of salt mixture (i.e. 1.25% instead of 2.50%) with the addition of 0% and 1.5% $CaNa_2EDTA$. The test group showed a reduced weight gain, but there was no distinct difference in general condition of the animals (Yang, 1964).

Groups of five male rats were given 250, 400 or 500 mg/kg bw disodium EDTA i.p. daily for three to 31 days; some groups were observed for another two weeks. At the 500 mg level all rats became lethargic and died within nine days, the kidneys being pale and swollen, with moderate dilatation of bowel and subserosal haemorrhages. Histological examination of a number of organs showed lesions only in the kidneys. Animals at the 400 mg level died within 14 days, kidney and bowel symptoms being similar to the 50 mg level. One rat at the 250 mg dose level showed haemorrhage of the thymus. All three groups showed varying degrees of hydrophic necrosis of the renal proximal convoluted tubules with epithelial sloughing: recovery occurred in all groups after withdrawal of disodium EDTA (Reuber and Schmieller, 1962).

Rabbit:

Eight groups of three rabbits were given either 0.1, 1, 10 or 20 mg/kg bw disodium EDTA i.v., or 50, 100, 500 or 1000 mg/kg bw orally for one month. All animals on the highest oral test level exhibited severe diarrhoea and died. In the other groups body weight, haemograms, urinary nitrogen and urobilinogen were unaffected. Histopathological examination of a number of organs showed degenerative changes in the liver, kidney, parathyroid and endocrine organs and oedema in muscle, brain and heart at all levels of treatment (Shibata, 1956).

Dog:

Four groups of one male and three female mongrels were fed diets containing 0, 50, 100 and 200 mg/kg bw $CaNa_2EDTA$ daily for 12 months. All appeared in good health, without significant change in blood cells, haemoglobin and urine (pH, albumin, sugar, sediment). Blood sugar, non-protein nitrogen and prothrombin time remained normal. Radiographs of ribs and of long bones showed no adverse changes at the 250 mg level. All dogs survived for one year. Gross and microscopic findings were normal (Oser et al., 1963).

2.2.3 Long-term/carcinogenicity studies

Mouse:

Groups of 50 male and 50 female B6C3F1 mice received trisodium EDTA (Na_3EDTA) in the diet at concentrations of 3,750 or 7,500 ppm for 103 weeks, followed by one week during which standard diet without EDTA was fed (NCI, 1977). A control group consisting of 20 mice of each sex received the standard diet of Wayne Lab Blox Meal. Food was available ad libitum and fresh food was provided three times per week.

Animals were examined for signs of toxicity twice per day, and were weighed and palpated for masses regularly (schedule not stated). Gross and microscopic pathological examinations were performed on animals found dead or moribund and on those sacrificed at the end of the study. Microscopic examinations were conducted on the following tissues and organs: skin, lymph nodes, mammary gland, salivary gland, bone marrow, trachea, lungs and bronchi, heart, thyroid, parathyroids, oesophagus, stomach, small intestine, liver, gallbladder, pancreas, spleen, kidneys, adrenals, urinary bladder, prostate or uterus, testis or ovary, brain and pituitary.

Survival rates were comparable among treated and control animals of both sexes. No treatment-related clinical signs of toxicity were noted during the study. Body weight gain was decreased in high dose males during the second year of the study (no statistical analysis). From the graphical representation of the data, it appears that the body weights in the high dose group were approximately 10% below that of controls during the last nine months of the study. In females, average body weights in treated groups were consistently lower than the average control body weight for most of the study period, however, the differences among the three groups were very slight. No tumours or non-neoplastic lesions attributable to treatment were observed.

Rat:

Rats were fed for 44 to 52 weeks on a diet containing 0.5% disodium EDTA without any deleterious effect on weight gain, appetite, activity and appearance (Krum, 1948).

In another experiment three groups of 10 to 13 males and females were fed a low-mineral diet (0.5% Ca and 0.013% Fe) with the addition of 0, 0.5 and 1% disodium EDTA for 205 days. At the 1% level some abnormal systems were observed: growth retardation of the males, lowered erythrocyte and leucocyte counts, a prolonged blood coagulation time, slightly but significantly raised blood calcium level, a significantly lower ash content of the bone, considerable erosion of the molars and diarrhoea. Gross and histological examination of the major organs revealed nothing abnormal. Rats fed for 220 days on an adequate mineral diet containing 1% disodium EDTA showed no evidence of dental erosion (Chan, 1964).

In a two-year study, five groups of 33 rats each were fed 0, 0.5, 1 and 5% disodium EDTA. The 5% group showed diarrhoea and consumed less food than the rats in other groups. No significant effects on weight gain were noted nor were blood coagulation time, red blood cell counts or bone ash adversely affected. The mortality of the animals could not be correlated with the level of disodium EDTA. The highest mortality rate occurred in the control group. Gross and microscopic examination of various organs revealed no significant differences between the groups (Yang, 1964).

Four groups of 25 male and 25 female rats were fed diets containing 0, 50, 125 and 250 mg/kg bw $CaNa_2EDTA$ for two years. Feeding was carried on through four successive generations. Rat were mated after 12 weeks' feeding and allowed to lactate for three weeks with one week's rest before producing a second litter. Ten male and 10 female rats of each group (F_1 generation) and similar F_2 and F_3 generation groups were allowed to produce two litters. Of the second litters of F_1, F_2, and F_3 generations only the control and the 250 mg/kg bw groups were kept until the end of two-years' study on the F_0 generation. This scheme permitted terminal observation to be made on rats receiving test diets for 0, 0.5, 1, 1.5 or 2 years in the F_3, F_2, F_1 and F_0 generations, respectively. No significant abnormalities in appearance and behaviour were noted during the 12 weeks of the post weaning period in all generations. The feeding experiment showed no statistically significant differences in weight gain, food efficiency, haematopoiesis, blood sugar, non-protein nitrogen, serum calcium, urine, organ weights and histopathology of liver, kidney, spleen, heart, adrenals, thyroid and gonads. Fertility, lactation and weaning were not adversely affected for each mating. Mortality and tumour incidence were unrelated to dosage level. The prothrombin time was normal. There was no evidence of any chelate effect on calcification of bone and teeth. Liver xanthine oxidase and blood carbonic anhydrase activities were unchanged (Oser et al., 1963).

Groups of 50 male and 50 female Fisher F344 rats received trisodium EDTA (Na_3EDTA) in the diet at concentrations of 3,750 or 7,500 ppm for 103 weeks, followed by one week during which standard diet without EDTA was fed (NCI, 1977). A control group consisting of 20 rats of each sex received the standard diet of Wayne Lab Blox Meal. Food was available ad libitum and fresh food was provided three times per week.

Animals were examined for signs of toxicity twice per day, and were weighed and palpated for masses regularly (schedule not stated). Gross and microscopic pathological

examinations were performed on animals found dead or moribund and on those sacrificed at the end of the study. Microscopic examinations were conducted on the following tissues and organs: skin, lymph nodes, mammary gland, salivary gland, bone marrow, trachea, lungs and bronchi, heart, thyroid, parathyroids, oesophagus, stomach, small intestine, liver, gallbladder, pancreas, spleen, kidneys, adrenals, urinary bladder, prostate or uterus, testis or ovary, brain and pituitary.

Survival was comparable among control and treated groups of male rats. There was a significant dose-related increase in survival in treated groups of females compared to controls. Body weights were comparable among treated and control groups, and there were no clinical signs of toxicity in treated animals. No tumours or non-neoplastic lesions attributable to treatment were observed (NCI, 1977).

2.2.4 Reproduction studies

Groups of six rats were maintained for 12 weeks on diets containing 0.5, 1 and 5% disodium EDTA. No deaths occurred and there were no toxic symptoms except diarrhoea and lowered food consumption at the 5% level. Mating in each group was carried out when the animals were 100 days old. Mating was repeated 10 days after weaning the first litters. Parent generation rats of 0, 0.5 and 1% levels gave birth to normal first and second litters. The animals given 5% failed to produce litters (Yang, 1964).

To elucidate possible teratogenic effects, daily doses of 20-40 mg EDTA per rat were injected i.m into pregnant rats at days six to nine, 10 to 15 and 16 to the end of pregnancy. A dose of 40 mg was lethal within four days but 20 mg was well tolerated, allowing normal fetal development; 40 mg injected during days six to eight or 10 to 15 produced some dead or malformed fetuses, especially polydactyly, double tail, generalized oedema or circumscribed head oedema (Tuchmann-Duplessis and Mercier-Parot, 1956).

In a four generation study, groups of rats received $CaNa_2EDTA$ at doses of 50, 125 or 250 mg/kg/day via the diet. No reproductive or teratogenic effects were observed in any of the three generations of offspring (Oser et al., 1963). This study is discussed in greater detail in Section 2.2.3 of this monograph.

Groups of pregnant Sprague-Dawley rats were fed Na_2EDTA in standard diet at levels of 2 or 3% from day 1 to 21 of gestation. Another group of pregnant rats received 3% Na_2EDTA in standard diet from day 6 to 14 of gestation. A third group received 3% Na_2EDTA and 1000 ppm zinc in the diet from day 6 to 21 of gestation. Controls received standard diet, which contained 100 ppm zinc. The number of mated animals per group ranged from 5 to 16. on day 21 of gestation fetuses were removed, fixed in Bouin's solution and stored in 70% ethanol. Fetuses were examined under a dissecting microscope for gross external abnormalities. Razor cut sections were examined for abnormalities of the eye and head. In rats fed 2% EDTA during pregnancy, litter size was normal and fetuses were alive. Gross congenital malformations were apparent in 7% of the treated in fetuses, compared to 0% in controls. In rats fed 3% EDTA during pregnancy, almost half of the implantation sites had dead fetuses or resorptions. Full term young were significantly smaller than controls and 100% of them were malformed. Maternal toxicity as manifested by diarrhoea was observed in rats fed 2 or 3% EDTA in the diet. Malformations included severe brain malformations, cleft palate, malformed digits, clubbed

legs and malformed tails. The detrimental effects of EDTA were prevented by supplementation of the diet with 1000 ppm zinc. These findings suggest that the teratogenic effects observed in rats fed EDTA at very high levels in the diet are due to zinc deficiency (Swenerton and Hurley, 1971).

Groups of pregnant CD rats were treated with Na_2EDTA via the diet at a dose of 954 mg/kg/day (3% in the diet; 42 rats), by gastric intubation at doses of 1250 mg/kg/day (split dose of 625 mg/kg twice/day; 22 rats) or 1500 mg/kg/day (split dose of 750 mg/kg twice/day; 8 rats), or by subcutaneous injection at a dose of 375 mg/kg/day (25 rats). Animals were dosed on gestation day 7 through 14. The number of control animals for each exposure route were: diet, 38; gavage, 20; subcutaneous injection, 14. Fetuses were removed at day 21 of gestation. One third of the fetuses from each litter (including all stunted fetuses and those with external malformations) were dissected and examined for visceral abnormalities. All fetuses surviving to the time of sacrifice were fixed and examined for skeletal malformations. Maternal toxicity as evidence by decreased food consumption, diarrhoea and diminished weight gain was observed in groups treated by all three dose routes. In the dietary exposure group, there were no maternal deaths, but there was a significant increase in fetal death and 71% of the fetuses were malformed. In the group administered 625 mg/kg/day by gavage, only 64% of the dams survived treatment. In those surviving, the number of fetal resorptions was similar to controls and 20.5% of the fetuses were malformed. Seven out of eight of the dams administered 750 mg/kg/day by gavage failed to survive. In the group administered EDTA by subcutaneous injection, 76% of the dams survived, the number of resorptions was significantly increased above control levels and the proportion of malformed fetuses was similar to controls. The types of malformations were consistent with those observed by Swenerton and Hurley (1971), although these former workers only evaluated external malformations. The results of this study indicate that the route of exposure to EDTA is an important factor in determining its lethality and teratogenicity (Kimmel, 1977).

Groups of 20 pregnant CD rats were administered EDTA, Na_2EDTA, Na_3EDTA, Na_4EDTA or $CaNa_2EDTA$ by gavage at a total dose of 1000 mg EDTA/kg/day in two divided doses per day during gestation day 7 through 14. All fetuses were subjected to gross examination. One third were sliced and examined for visceral abnormalities and the other two thirds were dissected, processed and examined for skeletal abnormalities. The incidence of diarrhoea was increased in all treated groups. Food intake was decreased in treated groups as was weight gain during the treatment period. Litter size and fetal mortality were unaffected by treatment in all groups. No treatment-related teratogenic effects were observed in any group (Schardein et al., 1981).

2.2.5 Special studies on embryotoxicity

Disodium EDTA injected at levels of 3.4, 1.7 and 0.35 mg/egg gave 40, 50 and 85% hatch, respectively. At the highest level, some embryos which failed to hatch showed anomalies (McLaughlin and Scott, 1964).

2.2.6 Special studies on genotoxicity

Na_3EDTA was tested for mutagenicity in the L5178Y tk^+/tk^- mouse lymphoma cell forward mutation assay. Two experiments were conducted with S9, and three without S9, using EDTA concentrations of up to 5,000 ug/ml. No mutagenicity was observed with or without S9 (McGregor et al., 1988).

Na_3EDTA was tested for mutagenicity in S. typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 as well as in E. coli WP uvrA, in the presence and absence of S9. Concentrations of up to 1 mg/plate were tested. No evidence of mutagenicity was found in either of these bacterial systems, by four independent laboratories (Dunkel et al., 1985).

2.2.7 Special studies on skin sensitization

Groups of 10 Hartley guinea pigs received topical application of Na_3EDTA, ethylene diamine (EDA) or DER epoxy resin (positive control) four times over 10 days to a shaved and depilated area on the back. Following a two week recovery period, animals received a challenge on the clipped flank. Animals originally treated with EDTA were not sensitized to EDTA. Animals originally treated with EDA were sensitized to EDA, but not to EDTA. The results of this study indicate a lack of sensitizing potential of EDTA and a lack of cross-sensitization between EDA and EDTA (Henck et al. 1985).

2.3 Observations in humans

Three comprehensive field trials have been carried out using NaFeEDTA as an iron fortificant in fish sauce (Garby and Areekul, 1974), off-white sugar (Viteri et al., 1983) curry powder (Ballot et al., 1989b). The salient features of these trials are listed in Table 3. All three trials were preceded by some estimate of the iron status of the population and care was taken to establish the acceptability and bioavailability of iron from the chosen vehicle prior to the trials (Garby and Areekul, 1974, Viteri et.al, 1983, Lamparelli et.al, 1987, Ballot et.al, 1989a). The choice of food vehicle in each case reflected the dietary habits of the population.

NaFeEDTA Fortified Fish Sauce (Garby and Areekul, 1974): Fortified fish sauce was provided for a period of one year to the population of a Thai village. The packed red cell volume (PCV) values before and after the fortification program showed a significant increase as compared to a control village supplied with unfortified fish sauce. The biggest mean change (+4.67) was seen in a sub-group of women who were anaemic at the start of the trial (initial PCV < 33). Although a similar sub-group of women in the control group also improved during the year (mean change +2.13) the increase in PCV in the fortified group was significantly greater. The same pattern was seen in both men and children with low initial PCV values.

In terms of iron nutrition the increase of 4.67 PCV units over initial values represents an increase of about 187 mg iron, in total body iron or an increase in daily absorption of about 0.5 mg over the duration of the trial (1 year). This is 64% of the expected increase in body iron of 0.8 mg per day calculated on the basis of an anticipated absorption of 8% and an assumed daily intake of 10 ml fortified fish sauce (10 mg Fe). Iron stores were not measured in this trial and the calculation does not take into account any absorbed iron which may have been laid down in stores. The calculated value therefore would be an underestimate of the total amount of iron

actually absorbed. Nevertheless it illustrates that fortification with NaFeEDTA is a highly effective method for improving iron status.

Overall this trial demonstrated that fortification of fish sauce at modest levels using NaFeEDTA is feasible, and that it can produce a significant improvement in iron status as assessed by a single simple criterion (PCV).

NaFeEDTA Fortified Sugar (Viteri et al., 1983): The design of this trial makes interpretation of the results difficult. The analysis is based on the comparative changes in iron status observed in four communities. Three (#13, #14, #16) were test sites, and one was a control site (#15). The initial iron status of individuals drawn from test community #14 was significantly worse than that of individuals from the other test communities and the control community (#15). Unfortunately compliance was poor in this community and also in test community #13. Furthermore seventy percent of the families in test communities number 13 and 14 used fortified sugar for only half of the time. The remaining 30% used it for 80% of the time. Finally, subjects with severe anaemia were given therapeutic iron to improve their iron status prior to the trial.

Despite the presence of these confounding factors, the haemoglobin values rose in both males and females after 20 months of fortification, although the values did not reach statistical significance. Only the children (5-12 years) in communities #13 and #16 showed a significant improvement in haemoglobin levels when compared to children in the control community #15 ($+2.2 \pm 1.7$ and $+2.2 \pm 1.5$ respectively vs $+ 1.6 \pm 1.2$ g/dl). The greater benefit observed in children may have resulted from the fact that sugar consumption was greater in children than in adults when considered relative to body weight. Mean serum ferritin which is a measure of the size of iron stores increased in each of the test communities, but not in the control community.

In conclusion it should be noted that the relatively modest improvement in iron status noted in this trial may also have been due, in part, to the fact that the fortification level was considerably less than in the other two trials (4.3 vs 10-15 and 7.7 mg/person/day).

NaFeEDTA Fortified Masala (Ballot et al., 1989a,b): The design of the most recent fortification trial differed from the earlier studies in that it was conducted in a single community with families randomly assigned to control and test groups. The groups were matched for iron status. It was also double-blinded and care was taken to ensure that cross-over between groups did not occur. Fortified or unfortified masala was distributed directly to each family. In addition to fortification the usual monitor of improving iron status (increasing haematocrit or haemoglobin and ferritin), an attempt was made to estimate the total body iron (in mg) in each individual by using a composite of haemoglobin concentration, percent saturation of transferrin and serum ferritin. This comprehensive index of iron nutrition made it possibly to compare subjects with wide variations in iron status and thus to assess both the beneficial and potentially adverse effects of additional iron i.e. development of iron overload (Cook et al., 1986).

Significant improvement in body iron as assessed by the index was detectable in the group of women receiving fortified masala after one year of the program. This improvement continued during the second year when the rise in haemoglobin concentration became significantly greater than in the control group. The prevalence of iron deficiency dropped dramatically in the women receiving fortified masala. Iron deficiency anaemia was detected in 22% of individuals at the start of the study, but only to 4.9% after two years. The most significant improvement in iron status was noted in women who entered the trial with iron

deficiency (especially in those with anaemia). They showed an increase in calculated body iron of 505 mg which is equivalent to the absorption of an additional 0.7 mg iron/day. The latter figure is close to the predicted improvement in iron balance of 0.8 mg daily based on isotopic absorption studies using NaFeEDTA fortified masala (Lamparelli et al., 1987).

In iron replete males the rise in calculated body iron was modest and only reached significance in alcohol abusers receiving fortified masala. This suggests that iron replete males are unlikely to accumulate excessive amounts of iron under these fortification conditions.

3. COMMENTS

Iron from NaFeEDTA is dissociated from the EDTA moiety prior to absorption and there is convincing evidence that iron chelated by EDTA (NaFeEDTA) is available for absorption via the physiologically regulated pathways responsible for iron uptake. In humans up to 25% of the iron in orally administered NaFeEDTA is absorbed. By contrast, only 5% or less of the EDTA from orally administered EDTA is absorbed. EDTA is eliminated in urine and faeces within 24 hours of oral or intravenous dosing with NaFeEDTA. There is no evidence that EDTA undergoes biotransformation.

Iron from NaFeEDTA equilibrates with food iron and joins the non-haem iron pool. Absorption studies in humans indicate that the EDTA moiety in $Na_2FeEDTA$ protects iron from the effects of inhibitory ligands in foods. When inhibitors are present, iron derived from NaFeEDTA is 2 to 3 times more available than it is from ferrous salts or food iron. Iron in NaFeEDTA exchanges with the nonhaem iron in the diet and the EDTA moiety also enhances the latter's bioavailability about 2-fold. The use of NaFeEDTA as an iron fortificant therefore holds promise for populations consuming diets of low iron bioavailability. Its major application will be in developing countries where the diets are largely cereal based. In this setting an absorption of 8 to 10% of both the added fortification iron and the intrinsic food iron can be expected. Thus the daily intake of food fortified with 10 mg of iron as NaFeEDTA would increase iron absorption in iron deficient subjects by at least 0.8 mg/day.

The influence of NaFeEDTA on metal biochemistry and nutrition has been carefully studied in both laboratory animals and humans and it can be concluded that the use of NaFeEDTA as a food fortificant would have no detrimental effect on the biochemistry or nutrition or metabolism of Ca, Cu, Zn or Mg. In some situations, fortifying foods with NaFeEDTA could have a beneficial effect on Zn nutrition by improving Zn absorption.

NaFeEDTA has not been evaluated in toxicology studies, however, several studies have been conducted using sodium and calcium EDTA complexes. It has been convincingly demonstrated in metabolism studies, that the EDTA and metal moieties from NaFeEDTA as well as calcium and sodium EDTA complexes, are dissociated prior to absorption. This provides a sound scientific basis for using the results from feeding studies using sodium and calcium EDTA complexes in evaluating the toxicology of NaFeEDTA.

Toxic effects of EDTA complexes in laboratory animals have only been reported following the injection of high doses, with the kidney being the main target organ. Toxic effects in feeding studies have only been observed in rats fed low mineral diets. In feeding studies using rats (12 to 52 weeks), rabbits (one month) and dogs (12 months) given diets containing a normal mineral complement, no adverse effects were observed at dose levels of 50 mg EDTA/kg bw/day (rat), 500 mg/kg (rabbit) or 200 mg/kg (dog). The no-observed-effect level (NOEL) in a 52 week study in which rats were fed a low mineral diet was 0.5% in the diet, or 250 mg EDTA/kg bw/day. In a long-term cancer bioassay in mice conducted by NCI since the last

JECFA review, reduced body weight gain was observed in males in the high dose group (1125 mg EDTA/kg bw/day), with only a slight probably non-significant decrease in body weight gain at the lower dose of 562.5 mg EDTA/kg bw/day. In two two-year rat studies, one of which was conducted by NCI since the time of the last JECFA review, no adverse effects were observed at the highest dose levels tested of 250 and 375 mg EDTA/kg bw/day, respectively. In a third two-year study in rats, diarrhoea and reduced food consumption were apparent in animals receiving a dose of 2500 mg EDTA/kg bw/day. The NOEL in this study was 1% in the diet, or 500 mg EDTA/kg bw/day. The findings in the two year studies are consistent with the findings from shorter term studies in which animals received diets containing a normal mineral complement. Teratogenic effects have been observed in rats fed high doses of some EDTA metal complexes, however, these effects have been attributed to Zn deficiency and are not relevant to the doses of NaFeEDTA which would be associated with food fortification.

4. EVALUATION

Level causing no toxicological effect

The NOEL associated with feeding EDTA to rats in a diet containing a normal mineral balance is 1% in the diet, equivalent to 500 mg EDTA/kg bw/day.

The NOEL associated with feeding EDTA to rats in a mineral reduced diet is 0.5% in the diet, equivalent to 250 mg EDTA/kg bw/day.

Since NaFeEDTA is intended for use in developing countries the NOEL based on studies using mineral deficient diets may be appropriate in developing an ADI.

Estimate of acceptable daily intake for man

2.5 mg EDTA/kg bw/day

0.80 mg Fe/kg bw/day (as established by JECFA, 1983)

The fortification level will be 10 mg/Fe per person/day (0.2 mg/kg Fe/day in a 50 kg person). This is associated with an EDTA intake from NaFeEDTA of 67 mg/EDTA per person/day (1.34 mg/kg EDTA/day in a 50 kg person). Since NaFeEDTA enhances absorption of Fe from inorganic Fe salts, a promising fortification option is the combination of NaFeEDTA with an iron salt to reduce the intake of EDTA.

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Table 1
Comparison of Iron Absorption from Meals of Different Iron Bioavailability Fortified with Ferrous Sulphate or NaFeEDTA

	Components of Meal	Standardized Iron Absorption (%)[a] A $FeSO_4$	B NaFeEDTA	Ratio B/A	Reference
1.	Rice Milk	1.7	4.5	2.6	Viteri *et al.*, 1978
2.	Beans, Maize, Coffee	2.0	5.3	2.7	Viteri *et al.*, 1978
3.	Egyptian flat bread[b]	2.1	5.3	2.5	el Guindi *et al.*, 1988
4.	Bran	2.7	7.8	2.9	MacPhail *et al.*, 1981
5.	Beans, Plantain, Rice, Maize, Soy[c]	3.1	7.0	2.3	Layrisse and Martinez-Torres, 1977
6.	Rice	3.9	11.5	2.9	MacPhail and Bothwell, unpublished, 1992
7.	Maize Meal	4.0	8.2	2.1	MaPhail *et al.*, 1981
8.	Beans, Plantain, Rice, Maize, Soy, Orange Juice[c]	4.2	7.4	1.8	Layrisse and Martinez-Torres, 1977
9.	Beans, Plantain, Rice, Maize, Soy, Meat[c]	4.3	9.6	2.2	Layrisse and Martinez-Torres, 1977
10.	Potato	5.9	7.3	1.2	Lamparelli *et al.*, 1987
11.	Wheat	6.2	14.6	2.3	Martinez-Torres *et al.*, 1979
12.	Milk	10.2	16.8	1.6	Layrisse and Martinez-Torres, 1977
13.	Sweet Manioc	14.1	16.6	1.2	Martinez-Torres *et al.*, 1979
14.	Sugar cane Syrup[c]	33.1	10.8	0.3	Martinez-Torres *et al.*, 1979

[a] Geometric means standarized to a reference (Ferrous ascorbate) absorption of 40%
[b] A mixture of $FeSO_4$ and Na_2EDTA was used in this study.
[c] Comparison between $FeSO_4$ and NaFeEDTA not in the same individuals.

Table 2

Percentage Iron Absorption From Meals
Containing NaFe(III)EDTA

Vehicle	No. of Studies	Standardized Iron Absorption (Range) Reprints	References
Wheat	4	10.1 (5.3 - 14.6)	Martinez-Torres *et al.*, 1979 and el Guindi *et al.*, 1988
Maize	7	9.1 (7.6 - 12.0)	Martinez-Torres *et al.*, 1979 and MacPhail *et al.*, 1981
Cassava	3	13.5 (11.0 - 16.4)	Martinez-Torres *et al.*, 1979

Table 5

Outline of Field Trials Using NaFeEDTA to Fortify Various Food Vehicles

References	Garby and Areekul, 1974	Viteri, et al., 1983	Ballot, et al., 1989a,b
Geographical Region	Thailand	Central America	South Africa
Population Studied	Two rural villages	4 rural Guatemalan communities	Urban Indian Community in a Municipal Housing Estate
Design of Trial	Controlled (One Village) Not Blinded	Controlled (Community #15) Not Blinded	Controlled (Random allocation by families) Double-blinded
Sample Studies	Test Village (284) Control Village (330)	#13 - 186 #14 - 306 #15 - 234 #16 - 296 Severe anemics treated prior to trial	263 Families (672 Subjects) 129 Control Families 134 Fortified Families Hb < 9 g/dl excluded
Food Vehicle	Fish-sauce (Salt substitute) 30 g NaCl/l, 10 mg Fe/l Distributed by Village Head-man as required	Off-White Sugar Distribution: Sold to store keepers. Purchased by participants (Poor Compliance #13 and #14)	Masala (Curry powder) Distributed directly to families monthly. Free of charge
Consumption of Food Vehicle	10 - 15 ml/person/day	33 g/person/day Children highest consumption	5.5 g/person/day
Fe Absorption	8%	8%	10%
Level of Fortification and Intake	1mg Fe/ml 10 - 15 mg Fe/person/day	13 mg Fe/100 g 4.29 mg Fe/person/day	1.4 mg Fe/g 7.7 mg Fe/person/day
Acceptability	No changes	Barely perceptible yellowing	Slight darkening of food
Duration of Trial	12 months	20 months	24 months
% Abnormal Iron Status prior to trial	30 - 50 of population anemic 34 initial PCV below normal	Comm / Low PCV / Low Sat / Low Ferr #13 31 34 52 #14 43 58 72 #15 35 12 37 #16 21 23 34	Females / Males IDA 24 4 ID 53 24
Measurements taken	Packed Cell Volume (PCV)	Hemoglobin, PCV, %Sat, FEP, Serum Ferritin, Cu, Zn	Hemoglobin, %Sat, Serum Ferritin

IDA = Iron Deficiency Anemia, ID = Iron Deficiency, % Sat = % Saturation of Transferrin, FEP = Free Erythrocyte Protoporphyrin, PCV = Packed Cell Volume, Comm = Community

SODIUM IRON EDTA

1. EXPLANATION

Sodium iron EDTA (NaFeEDTA) has not previously been evaluated by the Joint FAO/WHO Expert Committee on Food Additives. However, disodium and calcium disodium EDTA were evaluated and a monograph was published in WHO Food Additive Series 5 (JECFA, 1974). The ADI based on $CaNa_2EDTA$ was established as 2.5 mg EDTA/kg body weight/day.

Data is presented herein which supports the contention that this ADI is also applicable to NaFeEDTA. The monograph has been updated, and relevant sections are reproduced below.

With respect to iron, a provisional maximum tolerable daily intake of 0.8 mg/kg/day was established by the Committee in the twenty-seventh report (JECFA, 1983). The view stated at the twenty-sixth meeting, that the tolerable daily intake should not be used as a guide for fortifying processed foods, was reiterated. No new information relating to iron toxicology is presented in this monograph.

It has been estimated that 500-600 million of the world's 5 billion inhabitants suffer from nutritional iron deficiency anaemia (MacPhail and Bothwell, 1992). Most of these individuals live in developing countries where the prevalence of iron deficiency anaemia may be as high as 60-70% in preschool children and 60-80% in pregnant women (Bothwell et al., 1979; Simmons and Gurney, 1980).

The physiologic and economic consequences of iron deficiency occur at all ages, although the most significant effect on the individual may vary depending on his or her stage of development. From the public health point of view, iron deficiency places a severe handicap on the productivity of society owing to the long term consequences of premature birth, impaired cognitive achievement and reduced ability to carry out physically demanding tasks.

Iron fortification of the diet is the only cost effective long term strategy for reducing the prevalence of iron deficiency in most developing countries (Cook and Reusser, 1983; MacPhail and Bothwell, 1992). A proposed strategy for iron fortification in developing countries involves the use of NaFeEDTA. Despite the continuing high prevalence of iron deficiency in many developing countries and 40 years of research, iron fortification is not practised in developing countries. There are many reasons why this is so, but one of the most important is the practical difficulty of adding bioavailable iron to food in a form that will ensure its absorption. It is against this background that NaFeEDTA merits further consideration. It has as not yet been used because there has been some concern about the safety of prolonged ingestion of EDTA owing to the possibility of interactions with other trace metals. Data supporting the safety of NaFeEDTA as a food fortificant in developing countries are presented in this monograph.

2. BIOLOGICAL DATA

2.1 Biochemical aspects

The biochemistry of EDTA metal complexes is inextricably tied to their chemical properties. An understanding of these chemical properties is essential in interpreting the biochemistry and toxicology of EDTA metal complexes. A brief discussion of the chemical properties of EDTA metal complexes is presented here to facilitate understanding of the material that follows.

Ethylenediaminetetraacetic acid (EDTA) is a hexadentate chelator capable of combining stoichiometrically with virtually every metal in the periodic table (Chaberck and Martell, 1959). With divalent or trivalent metal ions a neutral or anionic metal chelate results. The metal is largely prevented from reacting with competing anions and its solubility is greatly increased. The effectiveness of EDTA as a chelate for a particular metal ion is given by its stability constant with the metal ion. Chelation potential is affected by pH, the molar ratio of chelate to metal ion, and the presence of competing metal ions capable of forming complexes with EDTA (Plumb et al., 1950; Martel, 1960; Hart, 1984). The stability constants for different metal-EDTA complexes vary considerably and any metal which is capable of forming a strong complex with EDTA will at least partially displace another metal.

Of the nutritionally important metals, Fe^{3+} has the highest stability constant (log k of 25.1), followed by Cu^{2+} with 18.4, Zn^{2+} with 16.1, Fe^{2+} with 14.6, Ca^{2+} with 10.6, Mg^{2+} with 8.7 and Na^{+} with 1.7 (West and Sykes, 1960). The situation is somewhat complicated by each metal having an optimum pH for chelate formation ranging from pH 1 for Fe^{3+}, to pH 3 for Cu^{2+}, pH 4 for Zn^{2+}, pH 5 for Fe^{2+}, pH 7.5 for Ca^{2+}, and pH 10 for Mg^{2+} (West and Sykes, 1960). When NaFeEDTA is ingested with foods, the Fe^{3+} ion would be expected to remain firmly bound to the EDTA moiety during passage through the gastric juice, but could be exchanged for Cu^{2+}, Zn^{2+}, Fe^{2+} or Ca^{2+} in the duodenum. Similarly when Na_2EDTA and $Na_2CaEDTA$ are consumed with foods, the Na^{+} and Ca^{2+} ions would be predominantly exchanged in the gastric juice for Fe^{3+} ions, which could again in turn be exchanged for Cu^{2+}, Zn^{2+}, Fe^{2+} or Ca^{2+} further down the gastrointestinal tract. The extent to which the metal EDTA complexes form is dependent on the pH and the concentration of the competing metals as well as competing ligands. The lower stability constant and higher pH optimum of the Mg-EDTA chelate make reaction with this metal less likely.

An appreciation of the chelating properties of EDTA with respect to iron provide the basis of our understanding of the observed effects of EDTA on food iron absorption. Ferric food iron is poorly absorbed by human beings because it is precipitated from solution above pH 3.5 unless suitable complexing agents are present. It may therefore be partially insoluble in the upper small intestine where most nonhaem iron is absorbed (Conrad and Schade, 1968; MacPhail et al., 1981). When EDTA is present in a meal, iron (primarily Fe^{3+}) remains complexed with EDTA under the acidic conditions prevailing in the stomach. The chelate holds the iron in solution as the pH rises in the upper small intestine, but the strength of the complex is progressively reduced allowing at least partial exchange with other metals and the release of some of the iron for absorption. There is convincing evidence that iron chelated by EDTA (NaFeEDTA) is available for absorption via the physiologically regulated pathways responsible for iron uptake (Candela et al., 1984). The results of absorption studies with NaFeEDTA

indicate that iron is dissociated from the EDTA moiety prior to absorption. The results of these studies are summarized in Section 2.1.1.

2.1.1 Absorption, distribution and excretion

Absorption and excretion of Fe from NaFeEDTA - injection studies

When NaFeEDTA is injected intravenously into rats most of the iron (70% - 90%) is lost through the urine within 24 hours (Najarajan et al., 1964; Anghileri, 1967). A small proportion enters the physiological iron pool destined primarily for haemoglobin synthesis probably because of the slow release of iron to the iron transport protein, transferrin, in the circulation (Bates et al., 1967). After intramuscular or intraperitoneal injection a greater proportion of the iron is available for physiological exchange with compartments in the bone marrow and liver. The longer contact time between transferrin and EDTA, allows for greater transfer of iron from the chelate to the physiological transport protein (Rubin et al., 1970).

FeEDTA administered intravenously to humans was almost quantitatively excreted in urine (Lapinleimu and Wegelius, 1959).

Absorption and excretion of Fe from NaFeEDTA - oral studies

Human iron deficiency anaemia was successfully treated with FeEDTA given orally with 84% of labelled FeEDTA excreted in the faeces and none in the urine. Red cells, however, contained labelled Fe and reticulocytosis occurred (Will and Vilter, 1954).

Studies carried out in swine using a dual labelled $Na^{55}Fe[2\text{-}^{14}C]EDTA$ preparation demonstrated rapid transfer of ^{55}Fe to the plasma with a peak at 1 hour and subsequent incorporation of 4.6% of the administered dose into circulating haemoglobin (Candela et al., 1984). A small fraction (0.3%) of the ^{55}Fe administered was excreted in the urine. In contrast to the ^{55}Fe only a small percentage of the ^{14}C could be detected in the plasma at any time. Absorption occurred over an extended period (5-20 hours). A total of about 5% of the ^{14}C labelled EDTA was eventually absorbed in the duodenum and jejunum and quantitatively excreted in the urine.

In a parallel experiment when 5 mg Fe as $Na^{59}FeEDTA$ was given to six fasting human volunteers, mean radioiron absorption as measured by red blood cell utilization was 12.0% (Candela et al., 1984). Only 0.3% of the administered dose of iron was excreted in the urine. The studies demonstrate that Fe and EDTA are absorbed independently when NaFeEDTA is administered by mouth.

Similar conclusions were reached in an earlier human absorption study carried out by MacPhail et al. (1981). $Na^{59}FeEDTA$ was administered to human volunteers. Between 3 and 25% of the ^{59}Fe was absorbed, but less than 1% of the administered ^{59}Fe appeared in the urine over the subsequent 24 hours. All ^{59}Fe absorbed in the form of the intact $Na^{59}FeEDTA$ complex would be expected to be excreted in the urine within 24 hours (based on the results of Najarajan et al., 1964 and Anghileri, 1967) demonstrating again that most of the iron is released from the EDTA complex before absorption. Similar conclusions have been reached with another iron

chelator (nitrilotriacetic acid), the properties of which have been studied extensively in experimental animals (Simpson and Peters, 1984).

Absorption and excretion of EDTA from EDTA metal chelates

Rat:

^{14}C-labelled $CaNa_2EDTA$, when fed to rats in doses of 50 mg/kg bw, was absorbed only to an extent of 2 to 4%; 80 to 90% of the dose appeared in the faeces within 24 hours, and absorption was still apparent at 48 hours. At the low pH of the stomach the calcium chelate is dissociated with subsequent precipitation of the free acid (EDTA), and this is only slowly redissolved in the intestine (Foreman et al., 1953).

In feeding experiments, in rats receiving disodium EDTA at dietary levels of 0.5, 1.0 and 5.0%, the faeces contained 99.4, 98.2 and 97.5% of the excreted material (Yang, 1964).

Similar experiments conducted also in rats gave essentially the same results. Thirty-two hours after a single dose of 95 mg disodium EDTA/rat, 93% was recovered from the colon. After doses of 47.5, 95.0 and 142.5 mg disodium EDTA the amount of EDTA recovered in the urine was directly proportional to the dose given, suggesting that EDTA was absorbed from the gastrointestinal tract by passive diffusion. The motility of the intestine was not affected by the compound (Chan, 1964).

When 200 mg $CaNa_2EDTA$ was introduced into the duodenum of rats an absorption rate of 6.5 to 26% was observed (Srbrova and Teisinger, 1957).

The maximum radioactivity in the urine after application of ^{14}C-labelled $CaNa_2EDTA$ to the skin was only 10 ppm (0.001%) (Foreman and Trujillo, 1954).

Human:

Experiments in man also revealed poor absorption; only 2.5% of a 3 g dose given was excreted in the urine (Srbrova and Teisinger, 1957). These authors also confirmed the dissociation of the calcium chelate in the stomach. A dose of 1.5 mg of ^{14}C-labelled $CaNa_2EDTA$ given in a gelatine capsule to normal healthy men was absorbed to an extent of 5% (Foreman et al., 1954).

The absorption of the EDTA moiety from orally administered NaFeEDTA has not been measured directly in humans. However physicochemical considerations indicate that EDTA absorption from NaFeEDTA would be similar to that from other metal complexes, such as $CaNa_2EDTA$ and CrEDTA. As described above, poor absorption of the intact NaFeEDTA can be inferred from the measurements of urinary radioiron excretion after the oral administration of $Na^{59}FeEDTA$ made by MacPhail and coworkers (1981).

Similar results have been obtained with a tightly bound chelate, ^{51}CrEDTA from which any released metal is very poorly absorbed (Bjarnason et al., 1983; Aabakken and Osnes, 1990). Only 1-5% of a dose of ^{51}CrEDTA given in a fasting state is absorbed by the healthy intestinal

mucosa. In the presence of disorders of the gastrointestinal tract the absorption may be doubled. The ^{51}CrEDTA that is absorbed appears to be taken up through intercellular junctions as the intact complex. The amount absorbed has been used as a measure of the integrity of the bowel mucosa.

In summary, most of the iron in NaFeEDTA is released to the physiological mucosal uptake system before absorption. Only a very small fraction of the NaFeEDTA complex (less than 1%) is absorbed intact and this is completely excreted in the urine. An additional small fraction (less than 5%) of the EDTA moiety is absorbed, presumably bound to other metals in the gastrointestinal tract, and is also completely eliminated in the urine.

Bioavailability of iron from NaFeEDTA

The results of iron absorption studies comparing the bioavailability of iron from $FeSO_4$ and NaFeEDTA fortified foods are listed in Table 1. For purposes of comparison the individual absorption values have been standardized to a reference absorption of 40% to remove the influence of varying iron requirements in different subjects. A reference absorption value of 40% is assumed to represent borderline iron deficiency (Hallberg et al., 1978). The bioavailability of iron from $FeSO_4$ varies over a wide range and correlates with the relative proportions of enhancers and inhibitors known to be present in the meals. In contrast, the absorption of iron from NaFeEDTA eaten with identical meals varies only two to three fold. More iron was absorbed from the meals containing NaFeEDTA in all but one case in which Na_2EDTA and $FeSO_4$ were eaten with sugar cane syrup (see Table 1). Enhanced bioavailability was most marked in meals with poor $FeSO_4$ bioavailability ($FeSO_4$ absorptions less than 4%). Between 2.1 to 2.9 times as much iron was absorbed under such circumstances. This point is exemplified by the results of the study by Viteri *et al.* (1978) (see Table 1) in which iron absorption from a NaFeEDTA-fortified meal of beans, maize, and coffee was 2.7 times greater than that from the same meal containing $FeSO_4$ (Viteri et al., 1978).

The absorption of Fe from NaFeEDTA has been studied in a wide variety of meals. Comparisons with iron absorption from simple iron salts have not always been made. However, some studies provide useful information about the suitability of three staple food items as potential vehicles for fortification with NaFeEDTA. This information is summarized in Table 2. Some studies listed in Table 1 have been included under the appropriate categories (all values are corrected to 40% reference absorption, or a serum ferritin of 27 μg/l). It is evident that approximately 10% of the fortification iron added would be absorbed by iron deficient individuals if these staple foods were used as the vehicle for delivering the fortificant.

Effect of NaFeEDTA on bioavailability of Intrinsic Food Iron

Conclusions drawn from much of the experimental work on food iron absorption and iron fortification are based on the observation that soluble iron added to a meal and the intrinsic nonhaem food iron behave as a common pool, which is equally susceptible to enhancers and inhibitors of iron absorption present in the meal (Cook et al., 1972; Hallberg and Bjorn-Rasmussen, 1972); NaFeEDTA shares this property. When Na^{59}FeEDTA was added to meals containing foods labelled intrinsically with ^{55}Fe, the ratio between the proportions of iron absorbed from the two sources was close to unity (Layrisse and Martinez-Torres, 1977; Matrinez-Torres et al., 1979; MacPhail et al., 1981), with the exception of one study in which

$Na^{59}FeEDTA$ fortified sugar was sprinkled onto ^{55}Fe-labelled maize immediately before it was eaten (MacPhail et al., 1981). These results indicate that the $Na^{59}FeEDTA$ equilibrates with the common pool, since without such equilibration, the amount of food iron absorbed would be much lower than the amount absorbed from NaFeEDTA (MacPhail et al., 1981). Inadequate mixing of the NaFeEDTA-fortified sugar with the maize meal probably accounted for the lack of equilibration in the one inconsistent study reported by MacPhail et al. (1981). These results reveal another important property of NaFeEDTA. Equilibration of NaFeEDTA with the common pool iron improves the bioavailability of the intrinsic food iron as well. Therefore NaFeEDTA improves iron balance by supplying iron in a form less affected by dietary inhibitors, but also improves the absorption of nonhaem iron in the meal derived from other sources.

This point is further illustrated by the results of a number of studies which demonstrate that the positive effects of EDTA on iron absorption are shared by other elements of the common pool, such as another iron salt added to the meal. When $FeSO_4$ and NaFeEDTA were fed to humans on separate days in the same type of meal (maize porridge), iron absorption from the NaFeEDTA fortified meal was significantly better. However the iron from $FeSO_4$ was as well absorbed as that from NaFeEDTA when they were fed together in the same meal (MacPhail et al., 1981; Martinez-Torres et al., 1979). More direct evidence of reciprocal exchange between food iron and iron added as NaFeEDTA was provided by experiments in which subjects were given maize porridge fortified with equimolar quantities of $^{59}FeSO_4$ and $Na^{55}FeEDTA$ (McPhail et al., 1981). The ratio between the two isotopes was almost the same in the meal and the urine. This implies that exchange of iron between $FeSO_4$ and NaFeEDTA must occur before absorption of the chelate, since only the small amount of iron (less than 1%) absorbed as the intact chelate would subsequently appear in the urine (for explanation see section 2.1).

The effect of Na_2EDTA on iron absorption

Na_2EDTA is widely used as a food additive to prevent oxidative damage by free metals. Since Na_2EDTA readily chelates iron in the gut to form NaFeEDTA, its effect on iron absorption is of interest. In a recent study (el Guindi et al., 1988) Na_2EDTA was added, together with an equimolar quantity of iron as $FeSO_4$, to bread with a high concentration of phytate (an inhibitor of iron absorption). The combination was associated with a 2.6x enhancement in iron absorption when compared with results with $FeSO_4$ used alone. Mean percentage iron absorption was approximately equivalent to that reported in other similar studies using NaFeEDTA. It is evident that the same effect on iron absorption can be achieved in meals containing compounds that inhibit iron absorption by adding Na_2EDTA and a soluble iron salt as is the case for adding NaFeEDTA.

The effects of Na_2EDTA on iron absorption appear to be influenced by the molar ratio of EDTA to iron. Earlier work suggested that increasing the molar ratio of Na_2EDTA to Fe was associated with a progressive reduction in iron absorption (Cook and Monsen, 1976). These observations have been extended recently (MacPhail and Bothwell, unpublished data, 1992). Iron absorption from a series of rice meals containing Na_2EDTA and iron in a molar ratio of 1:1 was compared to rice containing Na_2EDTA and iron in molar ratios (EDTA:Fe) ranging from 0:1 to 4:1. Statistically significant enhancement of absorption occurred at ratios of Fe:EDTA between 1:4 and 1:1. The enhancing effect of EDTA on iron absorption appeared to be maximal at a molar ratio (EDTA:Fe) of approximately 1:2, not 1:1 as previously assumed. At this molar

ratio over three times as much iron was absorbed from the EDTA containing meal as was the case for the control meal containing no EDTA.

Distribution

After parenteral administration to rats, 95 to 98% of injected ^{14}C-labelled $CaNa_2EDTA$ appeared in the urine within six hours. All the material passed through the body unchanged. Peak plasma levels were found approximately 50 minutes after administration. Less than 0.1% of the material was oxidized to $^{14}CO_2$, and no organs concentrated the substance. After i.v. injection, $CaNa_2EDTA$ passed rapidly out of the vascular systems to mix with approximately 90% of the body water, but did not pass into the red blood cells and was cleared through the kidney by tubular excretion as well as glomerular filtration (Foreman et al., 1953). The same was also found in man using ^{14}C-labelled $CaNa_2EDTA$. Three thousand milligrams were given i.v. to two subjects and were almost entirely excreted within 12 to 16 hours (Srbrova and Teisinger, 1957). These results indicate that intact $CaNa_2EDTA$, and presumably other EDTA metal complexes are rapidly excreted and do not accumulate.

2.1.2 Biotransformation

Neither the iron or EDTA moiety of NaFeEDTA undergoes biotransformation. Evidence for this conclusion comes from studies discussed in the previous section which indicated that both EDTA and iron are excreted unchanged following ingestion of NaFeEDTA.

2.1.3 Influence of EDTA compounds on the biochemistry of metals

EDTA removes about 1.4% of the total iron from ferritin at pH 7.4 to form an iron chelate (Westerfeld, 1961). Transfer of Fe from Fe-transferrin to EDTA in vitro occurs at a rate of less than 1% in 24 hours. In vivo studies in rabbits demonstrated transfer of iron only from FeEDTA to transferrin and not the reverse. It appeared that tissue iron became available to chelating agents including EDTA only when an excess of iron was present (Cleton et al., 1963). Equal distribution between a mixture of EDTA and siderophilin was obtained only at EDTA:siderophilin ratios of 20-25:1 (Rubin, 1961).

Addition of 1% Na_2EDTA to a diet containing more than optimal amounts of iron and calcium lowered the absorption and storage or iron in rats and increased the amount present in plasma and urine. The metabolism of calcium, however, was apparently unaffected (Larsen et al., 1960). A diet containing 0.15 mg of iron, 4.26 of calcium and 1 mg of EDTA per rat (equivalent to 100 ppm (0.01%) in the diet) for 83 days had no influence on calcium and iron metabolism, e.g. the iron content of liver and plasma (Hawkins et al., 1962).

Cu absorption and retention were improved at 500 mg EDTA/kg but not at 200 mg or 1000 mg EDTA/kg (Hurrell et al., 1992). Apart from a very small increase in urinary Cu excretion, dietary EDTA had no influence on Cu metabolism.

$CaNa_2EDTA$ increased the excretion of zinc (Perry and Perry, 1959), and was active in increasing the availability of zinc in soybean containing diets to poults (Kratzer et al., 1959). $CaNa_2EDTA$ enhanced the excretion of Co, Hg, Mn, Ni, Pb, Ti and W (Foreman, 1961). The

treatment of heavy metal poisoning with $CaNa_2EDTA$ has become so well established that its use for more commonly seen metal poisonings, e.g. lead, is no longer reported in the literature (Foreman, 1961). EDTA could not prevent the accumulation of ^{90}Sr, ^{106}Ru, ^{141}Ba and ^{226}Ra in the skeleton. ^{91}Y , ^{239}Pu and ^{238}U responded fairly well to EDTA, the excretion being accelerated (Catsch, 1961).

Food fortification with NaFeEDTA may be expected to increase Zn and Cu absorption and retention but not Ca or Mg. A diet containing RDA quantities of each metal (800 mg Ca and, 350 Mg, 10 mg Zn, and 2 mg Cu) which was fortified with 10 mg Fe as NaFeEDTA would contain a 1.5 molar excess of EDTA over Zn, an 8-fold molar excess of EDTA over Cu, but 80 times less EDTA than Ca and 50 times less EDTA than Mg on a molar basis. The small quantity of chelate with respect to Ca and Mg would be unlikely to have any detrimental effect. Both NaFeEDTA and NaEDTA may increase the absorption and retention of Zn and Cu when added to low bioavailability diets. This conclusion is supported by experiments with turkey poults (Kratzer et al., 1959), chicks (Scott and Ziegler, 1963) and rats (Forbes, 1961) which have demonstrated that Zn bioavailability and animal growth is improved when Na_2EDTA is added at 150-300 mg/kg to animal rations based on soybean protein isolate. The enhancing effect of EDTA on zinc absorption in these studies can be explained by a combination of two factors. Firstly, EDTA forms soluble chelates with Zn from which the metal is potentially absorbable, and secondly, Zn is prevented from forming non-absorbable complexes with phytic acid. EDTA does not enhance Zn absorption when absorption inhibitors are absent from the meal as evidenced by the observation that Na_2EDTA (1000 mg/kg) improved Zn absorption in rats fed a casein-based diet with added phytic acid, but had no effect in the absence of phytic acid (Oberleas et al., 1966). Other chelating substances can also enhance Zn absorption from low bioavailability diets. Vohra and Kratzer (1964) compared the growth promoting effect of chelates with stability constants (log k) for Zn varying from 5.3 to 18.8 in turkey poults fed zinc deficient diets based on soy protein isolate. They found that ethylenediaminediacetic acid-dipropionic acid, hydroxyethyl-EDTA, and EDTA (stability constants 14.5, 14.5 and 16.1, respectively) were the most effective.

These earlier observations were made with Na_2EDTA. However, NaFeEDTA has been shown to have similar properties in a recent study (Hurrell et al., 1992). Zinc, copper and calcium balances were performed in rats fed low Zn (6.1 mg/kg) soybean based diets containing 36 mg/kg added Fe as either ferrous sulphate or NaFeEDTA. In some experimental groups additional Na_2EDTA was added to the diet containing NaFeEDTA to give dietary EDTA levels of 200, 500 and 1000 mg/kg. Changing the iron compound in the diet from ferrous sulphate to NaFeEDTA at a level of 200 mg/kg increased apparent Zn absorption, urinary Zn excretion and Zn retention significantly ($p < 0.05$), but caused no changes in Cu or Ca absorption or excretion. Increasing the dietary EDTA level to 500 mg/kg (molar ratio EDTA:Zn, 19:1) and 1000 mg/kg (molar ratio EDTA:Zn, 38:1) further increased both Zn absorption and urinary Zn excretion. At the highest dietary EDTA level (1000 mg/kg), Zn retention was significantly higher than with no dietary EDTA, but lower than with 500 mg/kg EDTA. This resulted from an increase in urinary excretion of Zn to 15.6% of intake. Similar results were obtained with a Zn-sufficient (30 mg/kg) soybean diets, but more EDTA was required to achieve optimal ratios for improved absorption.

The studies of Hurrell et al. (1992) demonstrate that an 11-fold molar excess of EDTA over Cu increased Cu absorption and retention but that neither a 4.5 nor 23-fold molar excess had a significant effect. A human diet containing the RDA for Zn and Cu which was fortified with 10 mg Fe as NaFeEDTA would be expected to contain a 1.5 molar excess of EDTA over Zn and an 8-fold molar excess of EDTA over Cu. NaFeEDTA fortification would therefore be expected to have very little effect on Zn and Cu balance. A small beneficial effect could occur in meals containing little Zn or Cu or large quantities of phytate.

The applicability of the observations made in experimental animals to human nutrition has been confirmed by recent observations made by Hurrell's group (Davidsson, Kastenmayer and Hurrell, unpublished data, 1992). The metabolism of Zn and Ca was studied using a stable isotope technique in 10 adult women fed a breakfast meal of bread rolls made from 100 g high extraction wheat flour and fortified with 5 mg Fe as $FeSO_4$ or NaFeEDTA. The test meals contained a 3.3 molar excess of EDTA over Zn but some 10-fold less EDTA than Ca. Changing the Fe fortification compound from ferrous sulphate to NaFeEDTA significantly increased ^{70}Zn absorption ($p < 0.05$) from this meal from 20.9% to 33.5%. Urinary ^{70}Zn excretion also rose from 0.3% to 0.9%. Calcium metabolism was similar with the two different iron compounds. Earlier studies using less precise methodology have led to similar conclusions. Solomons et al. (1979) reported that adding NaFeEDTA to a low bioavailability Guatemalan meal did not influence Zn absorption by human subjects. However, as these workers measured Zn absorption based on plasma Zn concentrations after ingesting 25 mg Zn with a meal, the molar concentration of EDTA was some 10-fold less than that of Zn and an improvement in Zn absorption would not be expected. Finally no significant changes in plasma Zn concentration were observed in field studies in which NaFeEDTA was used as a food fortificant over a two year period (Viteri et al., 1983, Ballot et al., 1989b).

2.1.4 Effects on enzymes and other biochemical parameters

EDTA had a lowering effect on serum cholesterol level when given orally or i.v. It may have acted by decreasing the capacity of serum to transport cholesterol (Gould, 1961). Disodium EDTA had a pyridoxin-like effect on the tryptophan metabolism of patients with porphyria or scleroderma, due to a partial correction of imbalance of polyvalent cations (Lelievre and Betz, 1961).

In vitro, 0.0033 M EDTA inhibited the respiration of liver homogenates and of isolated mitochondria of liver and kidney (Lelievre and Betz, 1961). The acetylation of sulphanilamide by a liver extract was also inhibited (Lelievre, 1960). EDTA stimulated glucuronide synthesis in rat liver, kidney and intestines but inhibited the process in guinea-pig liver (Pogell and Leloir, 1961; Miettinen and Leskinen, 1962). Of the heavy metal-containing enzymes, EDTA at a concentration of about 10^{-3} M inhibited aldehyde oxidase and homogentisinase. Succinic dehydrogenase, xanthine oxidase, NADH-cytochrome reductase and ceruloplasmin (oxidation of p-phenylenediamine) were not inhibited (Westerfeld, 1961). Disodium EDTA was found to be a strong inhibitor for δ-aminolevulinic acid dehydrogenase, 5.5×10^{-6} M causing 50% inhibition (Gibson et al., 1955). The i.p. injection of 4.2 mmol/kg bw (equivalent to 1722 mg/kg bw) $CaNa_2EDTA$ caused in rats an inhibition of the alkaline phosphatase of liver, prostate and serum up to four days depending on the dose administered; zinc restored the activity (Nigrovic, 1964).

In vitro, EDTA inhibited blood coagulation by chelating Ca. The complete coagulation inhibition of human blood required 0.65-1.0 mg/ml. The i.v. injection of 79-200 mg EDTA/rabbit had no effect on blood coagulation (Dyckerhoff et al., 1942).

I.v. injections of Na_2EDTA and $CaNa_2EDTA$ had some pharmacological effect on the blood pressure of cats; 0-20 mg/kg bw $CaNa_2EDTA$ (as Ca) produce a slight rise; 20-50 mg/kg, a biphasic response; and 50 mg/kg, a clear depression (Marquardt and Schumacher, 1957).

One per cent Na_2EDTA enhances the absorption of ^{14}C-labelled acidic, neutral and basic compounds (mannitol, inulin, decamethenium, sulphanilic acid and EDTA itself) from isolated segments of rat intestine, probably due to an increased permeability of the intestinal wall (Schanker and Johnson, 1961).

2.2 Toxicology studies

2.2.1 Acute toxicity studies

(a) Disodium EDTA

Animal	Route	LD_{50} (mg/kg bw)	References
Rat	oral	2 000 - 2 200	Yang, 1964
Rabbit	oral	2 300	Shibata, 1956
	i.v.	47[a]	Shibata, 1956

[a]Dose depending on the rate of infusion

(b) Ca-disodium EDTA

Animal	Route	LD_{50} (mg/kg bw)	References
Rat	oral	10 000 ± 740	Oser et al., 1963
Rabbit	oral	7 000 approx.	Oser et al., 1963
	i.p.	500 approx.	Bauer et al., 1952
Dog	oral	12 000 approx.	Oser et al., 1963

The oral LD_{50} in rats is not affected by the presence of food in the stomach or by pre-existing deficiency in Ca, Fe, Cu or Mn (Oser et al., 1963).

Oral doses of over 250 mg/animal cause diarrhoea in rats (Foreman et al., 1953).

There are many reports in the literature on kidney damage by parenteral over-dosage of CaEDTA. A review was given by Lechnit (1961). Lesions simulating "versene nephrosis" in man have also been produced in rats. Disodium EDTA in doses of 400-500 mg i.p. for 21 days caused severe hydropic degeneration of the proximal convoluted tubules of the kidneys. $CaNa_2EDTA$ produced only minimal focal hydropic changes in 58% of animals, disappearing almost two weeks after stopping the injections (Reuber and Schmieller, 1962).

2.2.2 Short-term studies

Rat:

Groups of five male rats received 250 or 500 mg/kg bw $CaNa_2EDTA$ i.p. daily for three to 21 days and some were observed for an additional two weeks. Weight gain was satisfactory and histology of lung, thymus, kidney, liver, spleen, adrenal, small gut and heart was normal except for mild to moderate renal hydropic change with focal subcapsular swelling and proliferation in glomerular loops at the 500 mg level. There was very slight involvement with complete recovery at the 250 mg level. Lesions were not more severe with simultaneous cortisone administration (Reuber and Schmieller, 1962).

Groups of three male and three female rats were fed for four months on a low mineral diet containing one-half the usual portion of salt mixture (i.e. 1.25% instead of 2.50%) with the addition of 0% and 1.5% $CaNa_2EDTA$. The test group showed a reduced weight gain, but there was no distinct difference in general condition of the animals (Yang, 1964).

Groups of five male rats were given 250, 400 or 500 mg/kg bw disodium EDTA i.p. daily for three to 31 days; some groups were observed for another two weeks. At the 500 mg level all rats became lethargic and died within nine days, the kidneys being pale and swollen, with moderate dilatation of bowel and subserosal haemorrhages. Histological examination of a number of organs showed lesions only in the kidneys. Animals at the 400 mg level died within 14 days, kidney and bowel symptoms being similar to the 50 mg level. One rat at the 250 mg dose level showed haemorrhage of the thymus. All three groups showed varying degrees of hydrophic necrosis of the renal proximal convoluted tubules with epithelial sloughing: recovery occurred in all groups after withdrawal of disodium EDTA (Reuber and Schmieller, 1962).

Rabbit:

Eight groups of three rabbits were given either 0.1, 1, 10 or 20 mg/kg bw disodium EDTA i.v., or 50, 100, 500 or 1000 mg/kg bw orally for one month. All animals on the highest oral test level exhibited severe diarrhoea and died. In the other groups body weight, haemograms, urinary nitrogen and urobilinogen were unaffected. Histopathological examination of a number of organs showed degenerative changes in the liver, kidney, parathyroid and endocrine organs and oedema in muscle, brain and heart at all levels of treatment (Shibata, 1956).

Dog:

Four groups of one male and three female mongrels were fed diets containing 0, 50, 100 and 200 mg/kg bw $CaNa_2EDTA$ daily for 12 months. All appeared in good health, without significant change in blood cells, haemoglobin and urine (pH, albumin, sugar, sediment). Blood sugar, non-protein nitrogen and prothrombin time remained normal. Radiographs of ribs and of long bones showed no adverse changes at the 250 mg level. All dogs survived for one year. Gross and microscopic findings were normal (Oser et al., 1963).

2.2.3 Long-term/carcinogenicity studies

Mouse:

Groups of 50 male and 50 female B6C3F1 mice received trisodium EDTA (Na_3EDTA) in the diet at concentrations of 3,750 or 7,500 ppm for 103 weeks, followed by one week during which standard diet without EDTA was fed (NCI, 1977). A control group consisting of 20 mice of each sex received the standard diet of Wayne Lab Blox Meal. Food was available ad libitum and fresh food was provided three times per week.

Animals were examined for signs of toxicity twice per day, and were weighed and palpated for masses regularly (schedule not stated). Gross and microscopic pathological examinations were performed on animals found dead or moribund and on those sacrificed at the end of the study. Microscopic examinations were conducted on the following tissues and organs: skin, lymph nodes, mammary gland, salivary gland, bone marrow, trachea, lungs and bronchi, heart, thyroid, parathyroids, oesophagus, stomach, small intestine, liver, gallbladder, pancreas, spleen, kidneys, adrenals, urinary bladder, prostate or uterus, testis or ovary, brain and pituitary.

Survival rates were comparable among treated and control animals of both sexes. No treatment-related clinical signs of toxicity were noted during the study. Body weight gain was decreased in high dose males during the second year of the study (no statistical analysis). From the graphical representation of the data, it appears that the body weights in the high dose group were approximately 10% below that of controls during the last nine months of the study. In females, average body weights in treated groups were consistently lower than the average control body weight for most of the study period, however, the differences among the three groups were very slight. No tumours or non-neoplastic lesions attributable to treatment were observed.

Rat:

Rats were fed for 44 to 52 weeks on a diet containing 0.5% disodium EDTA without any deleterious effect on weight gain, appetite, activity and appearance (Krum, 1948).

In another experiment three groups of 10 to 13 males and females were fed a low-mineral diet (0.5% Ca and 0.013% Fe) with the addition of 0, 0.5 and 1% disodium EDTA for 205 days. At the 1% level some abnormal systems were observed: growth retardation of the males, lowered erythrocyte and leucocyte counts, a prolonged blood coagulation time, slightly but significantly raised blood calcium level, a significantly lower ash content of the bone, considerable erosion of the molars and diarrhoea. Gross and histological examination of the major organs revealed nothing abnormal. Rats fed for 220 days on an adequate mineral diet containing 1% disodium EDTA showed no evidence of dental erosion (Chan, 1964).

In a two-year study, five groups of 33 rats each were fed 0, 0.5, 1 and 5% disodium EDTA. The 5% group showed diarrhoea and consumed less food than the rats in other groups. No significant effects on weight gain were noted nor were blood coagulation time, red blood cell counts or bone ash adversely affected. The mortality of the animals could not be correlated with the level of disodium EDTA. The highest mortality rate occurred in the control group. Gross and microscopic examination of various organs revealed no significant differences between the groups (Yang, 1964).

Four groups of 25 male and 25 female rats were fed diets containing 0, 50, 125 and 250 mg/kg bw $CaNa_2EDTA$ for two years. Feeding was carried on through four successive generations. Rat were mated after 12 weeks' feeding and allowed to lactate for three weeks with one week's rest before producing a second litter. Ten male and 10 female rats of each group (F_1 generation) and similar F_2 and F_3 generation groups were allowed to produce two litters. Of the second litters of F_1, F_2, and F_3 generations only the control and the 250 mg/kg bw groups were kept until the end of two-years' study on the F_0 generation. This scheme permitted terminal observation to be made on rats receiving test diets for 0, 0.5, 1, 1.5 or 2 years in the F_3, F_2, F_1 and F_0 generations, respectively. No significant abnormalities in appearance and behaviour were noted during the 12 weeks of the post weaning period in all generations. The feeding experiment showed no statistically significant differences in weight gain, food efficiency, haematopoiesis, blood sugar, non-protein nitrogen, serum calcium, urine, organ weights and histopathology of liver, kidney, spleen, heart, adrenals, thyroid and gonads. Fertility, lactation and weaning were not adversely affected for each mating. Mortality and tumour incidence were unrelated to dosage level. The prothrombin time was normal. There was no evidence of any chelate effect on calcification of bone and teeth. Liver xanthine oxidase and blood carbonic anhydrase activities were unchanged (Oser et al., 1963).

Groups of 50 male and 50 female Fisher F344 rats received trisodium EDTA (Na_3EDTA) in the diet at concentrations of 3,750 or 7,500 ppm for 103 weeks, followed by one week during which standard diet without EDTA was fed (NCI, 1977). A control group consisting of 20 rats of each sex received the standard diet of Wayne Lab Blox Meal. Food was available ad libitum and fresh food was provided three times per week.

Animals were examined for signs of toxicity twice per day, and were weighed and palpated for masses regularly (schedule not stated). Gross and microscopic pathological

examinations were performed on animals found dead or moribund and on those sacrificed at the end of the study. Microscopic examinations were conducted on the following tissues and organs: skin, lymph nodes, mammary gland, salivary gland, bone marrow, trachea, lungs and bronchi, heart, thyroid, parathyroids, oesophagus, stomach, small intestine, liver, gallbladder, pancreas, spleen, kidneys, adrenals, urinary bladder, prostate or uterus, testis or ovary, brain and pituitary.

Survival was comparable among control and treated groups of male rats. There was a significant dose-related increase in survival in treated groups of females compared to controls. Body weights were comparable among treated and control groups, and there were no clinical signs of toxicity in treated animals. No tumours or non-neoplastic lesions attributable to treatment were observed (NCI, 1977).

2.2.4 Reproduction studies

Groups of six rats were maintained for 12 weeks on diets containing 0.5, 1 and 5% disodium EDTA. No deaths occurred and there were no toxic symptoms except diarrhoea and lowered food consumption at the 5% level. Mating in each group was carried out when the animals were 100 days old. Mating was repeated 10 days after weaning the first litters. Parent generation rats of 0, 0.5 and 1% levels gave birth to normal first and second litters. The animals given 5% failed to produce litters (Yang, 1964).

To elucidate possible teratogenic effects, daily doses of 20-40 mg EDTA per rat were injected i.m into pregnant rats at days six to nine, 10 to 15 and 16 to the end of pregnancy. A dose of 40 mg was lethal within four days but 20 mg was well tolerated, allowing normal fetal development; 40 mg injected during days six to eight or 10 to 15 produced some dead or malformed fetuses, especially polydactyly, double tail, generalized oedema or circumscribed head oedema (Tuchmann-Duplessis and Mercier-Parot, 1956).

In a four generation study, groups of rats received $CaNa_2EDTA$ at doses of 50, 125 or 250 mg/kg/day via the diet. No reproductive or teratogenic effects were observed in any of the three generations of offspring (Oser et al., 1963). This study is discussed in greater detail in Section 2.2.3 of this monograph.

Groups of pregnant Sprague-Dawley rats were fed Na_2EDTA in standard diet at levels of 2 or 3% from day 1 to 21 of gestation. Another group of pregnant rats received 3% Na_2EDTA in standard diet from day 6 to 14 of gestation. A third group received 3% Na_2EDTA and 1000 ppm zinc in the diet from day 6 to 21 of gestation. Controls received standard diet, which contained 100 ppm zinc. The number of mated animals per group ranged from 5 to 16. on day 21 of gestation fetuses were removed, fixed in Bouin's solution and stored in 70% ethanol. Fetuses were examined under a dissecting microscope for gross external abnormalities. Razor cut sections were examined for abnormalities of the eye and head. In rats fed 2% EDTA during pregnancy, litter size was normal and fetuses were alive. Gross congenital malformations were apparent in 7% of the treated in fetuses, compared to 0% in controls. In rats fed 3% EDTA during pregnancy, almost half of the implantation sites had dead fetuses or resorptions. Full term young were significantly smaller than controls and 100% of them were malformed. Maternal toxicity as manifested by diarrhoea was observed in rats fed 2 or 3% EDTA in the diet. Malformations included severe brain malformations, cleft palate, malformed digits, clubbed

legs and malformed tails. The detrimental effects of EDTA were prevented by supplementation of the diet with 1000 ppm zinc. These findings suggest that the teratogenic effects observed in rats fed EDTA at very high levels in the diet are due to zinc deficiency (Swenerton and Hurley, 1971).

Groups of pregnant CD rats were treated with Na_2EDTA via the diet at a dose of 954 mg/kg/day (3% in the diet; 42 rats), by gastric intubation at doses of 1250 mg/kg/day (split dose of 625 mg/kg twice/day; 22 rats) or 1500 mg/kg/day (split dose of 750 mg/kg twice/day; 8 rats), or by subcutaneous injection at a dose of 375 mg/kg/day (25 rats). Animals were dosed on gestation day 7 through 14. The number of control animals for each exposure route were: diet, 38; gavage, 20; subcutaneous injection, 14. Fetuses were removed at day 21 of gestation. One third of the fetuses from each litter (including all stunted fetuses and those with external malformations) were dissected and examined for visceral abnormalities. All fetuses surviving to the time of sacrifice were fixed and examined for skeletal malformations. Maternal toxicity as evidence by decreased food consumption, diarrhoea and diminished weight gain was observed in groups treated by all three dose routes. In the dietary exposure group, there were no maternal deaths, but there was a significant increase in fetal death and 71% of the fetuses were malformed. In the group administered 625 mg/kg/day by gavage, only 64% of the dams survived treatment. In those surviving, the number of fetal resorptions was similar to controls and 20.5% of the fetuses were malformed. Seven out of eight of the dams administered 750 mg/kg/day by gavage failed to survive. In the group administered EDTA by subcutaneous injection, 76% of the dams survived, the number of resorptions was significantly increased above control levels and the proportion of malformed fetuses was similar to controls. The types of malformations were consistent with those observed by Swenerton and Hurley (1971), although these former workers only evaluated external malformations. The results of this study indicate that the route of exposure to EDTA is an important factor in determining its lethality and teratogenicity (Kimmel, 1977).

Groups of 20 pregnant CD rats were administered EDTA, Na_2EDTA, Na_3EDTA, Na_4EDTA or $CaNa_2EDTA$ by gavage at a total dose of 1000 mg EDTA/kg/day in two divided doses per day during gestation day 7 through 14. All fetuses were subjected to gross examination. One third were sliced and examined for visceral abnormalities and the other two thirds were dissected, processed and examined for skeletal abnormalities. The incidence of diarrhoea was increased in all treated groups. Food intake was decreased in treated groups as was weight gain during the treatment period. Litter size and fetal mortality were unaffected by treatment in all groups. No treatment-related teratogenic effects were observed in any group (Schardein et al., 1981).

2.2.5 Special studies on embryotoxicity

Disodium EDTA injected at levels of 3.4, 1.7 and 0.35 mg/egg gave 40, 50 and 85% hatch, respectively. At the highest level, some embryos which failed to hatch showed anomalies (McLaughlin and Scott, 1964).

2.2.6 Special studies on genotoxicity

Na_3EDTA was tested for mutagenicity in the L5178Y tk^+/tk^- mouse lymphoma cell forward mutation assay. Two experiments were conducted with S9, and three without S9, using EDTA concentrations of up to 5,000 ug/ml. No mutagenicity was observed with or without S9 (McGregor et al., 1988).

Na_3EDTA was tested for mutagenicity in S. typhimurium strains TA98, TA100, TA1535, TA1537 and TA1538 as well as in E. coli WP uvrA, in the presence and absence of S9. Concentrations of up to 1 mg/plate were tested. No evidence of mutagenicity was found in either of these bacterial systems, by four independent laboratories (Dunkel et al., 1985).

2.2.7 Special studies on skin sensitization

Groups of 10 Hartley guinea pigs received topical application of Na_3EDTA, ethylene diamine (EDA) or DER epoxy resin (positive control) four times over 10 days to a shaved and depilated area on the back. Following a two week recovery period, animals received a challenge on the clipped flank. Animals originally treated with EDTA were not sensitized to EDTA. Animals originally treated with EDA were sensitized to EDA, but not to EDTA. The results of this study indicate a lack of sensitizing potential of EDTA and a lack of cross-sensitization between EDA and EDTA (Henck et al. 1985).

2.3 Observations in humans

Three comprehensive field trials have been carried out using NaFeEDTA as an iron fortificant in fish sauce (Garby and Areekul, 1974), off-white sugar (Viteri et al., 1983) curry powder (Ballot et al., 1989b). The salient features of these trials are listed in Table 3. All three trials were preceded by some estimate of the iron status of the population and care was taken to establish the acceptability and bioavailability of iron from the chosen vehicle prior to the trials (Garby and Areekul, 1974, Viteri et.al, 1983, Lamparelli et.al, 1987, Ballot et.al, 1989a). The choice of food vehicle in each case reflected the dietary habits of the population.

NaFeEDTA Fortified Fish Sauce (Garby and Areekul, 1974): Fortified fish sauce was provided for a period of one year to the population of a Thai village. The packed red cell volume (PCV) values before and after the fortification program showed a significant increase as compared to a control village supplied with unfortified fish sauce. The biggest mean change (+4.67) was seen in a sub-group of women who were anaemic at the start of the trial (initial PCV < 33). Although a similar sub-group of women in the control group also improved during the year (mean change +2.13) the increase in PCV in the fortified group was significantly greater. The same pattern was seen in both men and children with low initial PCV values.

In terms of iron nutrition the increase of 4.67 PCV units over initial values represents an increase of about 187 mg iron, in total body iron or an increase in daily absorption of about 0.5 mg over the duration of the trial (1 year). This is 64% of the expected increase in body iron of 0.8 mg per day calculated on the basis of an anticipated absorption of 8% and an assumed daily intake of 10 ml fortified fish sauce (10 mg Fe). Iron stores were not measured in this trial and the calculation does not take into account any absorbed iron which may have been laid down in stores. The calculated value therefore would be an underestimate of the total amount of iron

actually absorbed. Nevertheless it illustrates that fortification with NaFeEDTA is a highly effective method for improving iron status.

Overall this trial demonstrated that fortification of fish sauce at modest levels using NaFeEDTA is feasible, and that it can produce a significant improvement in iron status as assessed by a single simple criterion (PCV).

NaFeEDTA Fortified Sugar (Viteri et al., 1983): The design of this trial makes interpretation of the results difficult. The analysis is based on the comparative changes in iron status observed in four communities. Three (#13, #14, #16) were test sites, and one was a control site (#15). The initial iron status of individuals drawn from test community #14 was significantly worse than that of individuals from the other test communities and the control community (#15). Unfortunately compliance was poor in this community and also in test community #13. Furthermore seventy percent of the families in test communities number 13 and 14 used fortified sugar for only half of the time. The remaining 30% used it for 80% of the time. Finally, subjects with severe anaemia were given therapeutic iron to improve their iron status prior to the trial.

Despite the presence of these confounding factors, the haemoglobin values rose in both males and females after 20 months of fortification, although the values did not reach statistical significance. Only the children (5-12 years) in communities #13 and #16 showed a significant improvement in haemoglobin levels when compared to children in the control community #15 ($+2.2 \pm 1.7$ and $+2.2 \pm 1.5$ respectively vs $+ 1.6 \pm 1.2$ g/dl). The greater benefit observed in children may have resulted from the fact that sugar consumption was greater in children than in adults when considered relative to body weight. Mean serum ferritin which is a measure of the size of iron stores increased in each of the test communities, but not in the control community.

In conclusion it should be noted that the relatively modest improvement in iron status noted in this trial may also have been due, in part, to the fact that the fortification level was considerably less than in the other two trials (4.3 vs 10-15 and 7.7 mg/person/day).

NaFeEDTA Fortified Masala (Ballot et al., 1989a,b): The design of the most recent fortification trial differed from the earlier studies in that it was conducted in a single community with families randomly assigned to control and test groups. The groups were matched for iron status. It was also double-blinded and care was t.ken to ensure that cross-over between groups did not occur. Fortified or unfortified masala was distributed directly to each family. In addition to fortification the usual monitor of improving iron status (increasing haematocrit or haemoglobin and ferritin), an attempt was made to estimate the total body iron (in mg) in each individual by using a composite of haemoglobin concentration, percent saturation of transferrin and serum ferritin. This comprehensive index of iron nutrition made it possibly to compare subjects with wide variations in iron status and thus to assess both the beneficial and potentially adverse effects of additional iron i.e. development of iron overload (Cook et al., 1986).

Significant improvement in body iron as assessed by the index was detectable in the group of women receiving fortified masala after one year of the program. This improvement continued during the second year when the rise in haemoglobin concentration became significantly greater than in the control group. The prevalence of iron deficiency dropped dramatically in the women receiving fortified masala. Iron deficiency anaemia was detected in 22% of individuals at the start of the study, but only to 4.9% after two years. The most significant improvement in iron status was noted in women who entered the trial with iron

deficiency (especially in those with anaemia). They showed an increase in calculated body iron of 505 mg which is equivalent to the absorption of an additional 0.7 mg iron/day. The latter figure is close to the predicted improvement in iron balance of 0.8 mg daily based on isotopic absorption studies using NaFeEDTA fortified masala (Lamparelli et al., 1987).

In iron replete males the rise in calculated body iron was modest and only reached significance in alcohol abusers receiving fortified masala. This suggests that iron replete males are unlikely to accumulate excessive amounts of iron under these fortification conditions.

3. COMMENTS

Iron from NaFeEDTA is dissociated from the EDTA moiety prior to absorption and there is convincing evidence that iron chelated by EDTA (NaFeEDTA) is available for absorption via the physiologically regulated pathways responsible for iron uptake. In humans up to 25% of the iron in orally administered NaFeEDTA is absorbed. By contrast, only 5% or less of the EDTA from orally administered EDTA is absorbed. EDTA is eliminated in urine and faeces within 24 hours of oral or intravenous dosing with NaFeEDTA. There is no evidence that EDTA undergoes biotransformation.

Iron from NaFeEDTA equilibrates with food iron and joins the non-haem iron pool. Absorption studies in humans indicate that the EDTA moiety in $Na_2FeEDTA$ protects iron from the effects of inhibitory ligands in foods. When inhibitors are present, iron derived from NaFeEDTA is 2 to 3 times more available than it is from ferrous salts or food iron. Iron in NaFeEDTA exchanges with the nonhaem iron in the diet and the EDTA moiety also enhances the latter's bioavailability about 2-fold. The use of NaFeEDTA as an iron fortificant therefore holds promise for populations consuming diets of low iron bioavailability. Its major application will be in developing countries where the diets are largely cereal based. In this setting an absorption of 8 to 10% of both the added fortification iron and the intrinsic food iron can be expected. Thus the daily intake of food fortified with 10 mg of iron as NaFeEDTA would increase iron absorption in iron deficient subjects by at least 0.8 mg/day.

The influence of NaFeEDTA on metal biochemistry and nutrition has been carefully studied in both laboratory animals and humans and it can be concluded that the use of NaFeEDTA as a food fortificant would have no detrimental effect on the biochemistry or nutrition or metabolism of Ca, Cu, Zn or Mg. In some situations, fortifying foods with NaFeEDTA could have a beneficial effect on Zn nutrition by improving Zn absorption.

NaFeEDTA has not been evaluated in toxicology studies, however, several studies have been conducted using sodium and calcium EDTA complexes. It has been convincingly demonstrated in metabolism studies, that the EDTA and metal moieties from NaFeEDTA as well as calcium and sodium EDTA complexes, are dissociated prior to absorption. This provides a sound scientific basis for using the results from feeding studies using sodium and calcium EDTA complexes in evaluating the toxicology of NaFeEDTA.

Toxic effects of EDTA complexes in laboratory animals have only been reported following the injection of high doses, with the kidney being the main target organ. Toxic effects in feeding studies have only been observed in rats fed low mineral diets. In feeding studies using rats (12 to 52 weeks), rabbits (one month) and dogs (12 months) given diets containing a normal mineral complement, no adverse effects were observed at dose levels of 50 mg EDTA/kg bw/day (rat), 500 mg/kg (rabbit) or 200 mg/kg (dog). The no-observed-effect level (NOEL) in a 52 week study in which rats were fed a low mineral diet was 0.5% in the diet, or 250 mg EDTA/kg bw/day. In a long-term cancer bioassay in mice conducted by NCI since the last

101

JECFA review, reduced body weight gain was observed in males in the high dose group (1125 mg EDTA/kg bw/day), with only a slight probably non-significant decrease in body weight gain at the lower dose of 562.5 mg EDTA/kg bw/day. In two two-year rat studies, one of which was conducted by NCI since the time of the last JECFA review, no adverse effects were observed at the highest dose levels tested of 250 and 375 mg EDTA/kg bw/day, respectively. In a third two-year study in rats, diarrhoea and reduced food consumption were apparent in animals receiving a dose of 2500 mg EDTA/kg bw/day. The NOEL in this study was 1% in the diet, or 500 mg EDTA/kg bw/day. The findings in the two year studies are consistent with the findings from shorter term studies in which animals received diets containing a normal mineral complement. Teratogenic effects have been observed in rats fed high doses of some EDTA metal complexes, however, these effects have been attributed to Zn deficiency and are not relevant to the doses of NaFeEDTA which would be associated with food fortification.

4. EVALUATION

Level causing no toxicological effect

The NOEL associated with feeding EDTA to rats in a diet containing a normal mineral balance is 1% in the diet, equivalent to 500 mg EDTA/kg bw/day.

The NOEL associated with feeding EDTA to rats in a mineral reduced diet is 0.5% in the diet, equivalent to 250 mg EDTA/kg bw/day.

Since NaFeEDTA is intended for use in developing countries the NOEL based on studies using mineral deficient diets may be appropriate in developing an ADI.

Estimate of acceptable daily intake for man

2.5 mg EDTA/kg bw/day

0.80 mg Fe/kg bw/day (as established by JECFA, 1983)

The fortification level will be 10 mg/Fe per person/day (0.2 mg/kg Fe/day in a 50 kg person). This is associated with an EDTA intake from NaFeEDTA of 67 mg/EDTA per person/day (1.34 mg/kg EDTA/day in a 50 kg person). Since NaFeEDTA enhances absorption of Fe from inorganic Fe salts, a promising fortification option is the combination of NaFeEDTA with an iron salt to reduce the intake of EDTA.

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70V

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Components of Meal		Standardized Iron Absorption (%)[a] A $FeSO_4$	B NaFeEDTA	Ratio B/A	Reference
1.	Rice Milk	1.7	4.5	2.6	Viteri *et al.*, 1978
2.	Beans, Maize, Coffee	2.0	5.3	2.7	Viteri *et al.*, 1978
3.	Egyptian flat bread[b]	2.1	5.3	2.5	el Guindi *et al.*, 1988
4.	Bran	2.7	7.8	2.9	MacPhail *et al.*, 1981
5.	Beans, Plantain, Rice, Maize, Soy[c]	3.1	7.0	2.3	Layrisse and Martinez-Torres, 1977
6.	Rice	3.9	11.5	2.9	MacPhail and Bothwell, unpublished, 1992
7.	Maize Meal	4.0	8.2	2.1	MaPhail *et al.*, 1981
8.	Beans, Plantain, Rice, Maize, Soy, Orange Juice[c]	4.2	7.4	1.8	Layrisse and Martinez-Torres, 1977
9.	Beans, Plantain, Rice, Maize, Soy, Meat[c]	4.3	9.6	2.2	Layrisse and Martinez-Torres, 1977
10.	Potato	5.9	7.3	1.2	Lamparelli *et al.*, 1987
11.	Wheat	6.2	14.6	2.3	Martinez-Torres *et al.*, 1979
12.	Milk	10.2	16.8	1.6	Layrisse and Martinez-Torres, 1977
13.	Sweet Manioc	14.1	16.6	1.2	Martinez-Torres *et al.*, 1979
14.	Sugar cane Syrup[c]	33.1	10.8	0.3	Martinez-Torres *et al.*, 1979

[a] Geometric means standarized to a reference (Ferrous ascorbate) absorption of 40%

[b] A mixture of $FeSO_4$ and Na_2EDTA was used in this study.

[c] Comparison between $FeSO_4$ and NaFeEDTA not in the same individuals.

Table 2

Percentage Iron Absorption From Meals
Containing NaFe(III)EDTA

Vehicle	No. of Studies	Standardized Iron Absorption (Range) Reprints	References
Wheat	4	10.1 (5.3 - 14.6)	Martinez-Torres *et al.*, 1979 and el Guindi *et al.*, 1988
Maize	7	9.1 (7.6 - 12.0)	Martinez-Torres *et al.*, 1979 and MacPhail *et al.*, 1981
Cassava	3	13.5 (11.0 - 16.4)	Martinez-Torres *et al.*, 1979

References	Garby and Areekul, 1974	Viteri, et al., 1983	Ballot, et al., 1989a,b
Geographical Region	Thailand	Central America	South Africa
Population Studied	Two rural villages	4 rural Guatemalan communities	Urban Indian Community in a Municipal Housing Estate
Design of Trial	Controlled (One Village) Not Blinded	Controlled (Community #15) Not Blinded	Controlled (Random allocation by families) Double-blinded
Sample Studies	Test Village (284) Control Village (330)	#13 - 186 #14 - 306 #15 - 234 #16 - 296 Severe anemics treated prior to trial	263 Families (672 Subjects) 129 Control Families 134 Fortified Families Hb < 9 g/dl excluded
Food Vehicle	Fish-sauce (Salt substitute) 30 g NaCl/l, 10 mg Fe/l Distributed by Village Head-man as required	Off-White Sugar Distribution: Sold to store keepers. Purchased by participants (Poor Compliance #13 and #14)	Masala (Curry powder) Distributed directly to families monthly. Free of charge
Consumption of Food Vehicle	10 - 15 ml/person/day	33 g/person/day Children highest consumption	5.5 g/person/day
Fe Absorption	8%	8%	10%
Level of Fortification and Intake	1mg Fe/ml 10 - 15 mg Fe/person/day	13 mg Fe/100 g 4.29 mg Fe/person/day	1.4 mg Fe/g 7.7 mg Fe/person/day
Acceptability	No changes	Barely perceptible yellowing	Slight darkening of food
Duration of Trial	12 months	20 months	24 months
% Abnormal Iron Status prior to trial	30 - 50 of population anemic 34 initial PCV below normal	Comm / Low PCV / Low Sat / Low Ferr #13 31 34 52 #14 43 58 72 #15 35 12 37 #16 21 23 34	Females / Males IDA 24 4 ID 53 24
Measurements taken	Packed Cell Volume (PCV)	Hemoglobin, PCV, %Sat, FEP, Serum Ferritin, Cu, Zn	Hemoglobin, %Sat, Serum Ferritin

IDA = Iron Deficiency Anemia, ID = Iron Deficiency. % Sat = % Saturation of Transferrin, FEP = Free Erythrocyte Protoporphyrin, PCV = Packed Cell Volume, Comm = Community

Appendix 17

WORLD HEALTH ORGANIZATION
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FOOD AND AGRICULTURE
ORGANIZATION
OF THE UNITED NATIONS

JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES
Forty-first meeting, Geneva, 9-18 February 1993

SUMMARY AND CONCLUSIONS

A Joint FAO/WHO Expert Committee on Food Additives (JECFA) meeting was held in Geneva, Switzerland, from 9 to 18 February 1993. The meeting was opened by Dr N.P. Napalkov, Assistant Director-General, on behalf of the Directors-General of the Food and Agriculture Organization of the United Nations and of the World Health Organization.

Professor R. Walker, School of Biological Sciences, University of Surrey, Guildford, Surrey, United Kingdom, acted as Chairman. Mrs I. Meyland, Senior Scientific Officer, National Food Agency, Ministry of Health, Søborg, Denmark, acted as Vice-Chairman.

Dr J. Paakkanen, Food Quality and Standards Service, Food Policy and Nutrition Division, Food and Agriculture Organization of the United Nations, acted as FAO Joint Secretary. Dr J.L. Herrman, International Programme on Chemical Safety, World Health Organization, acted as WHO Joint Secretary.

The present meeting was the forty-first of a series of similar meetings. The tasks before the Committee were to (a) further elaborate principles for evaluating the safety of food additives and contaminants; (b) undertake toxicological evaluations of certain food additives and contaminants and to review and prepare specifications for selected food additives; and (c) discuss and advise on matters arising from the Twenty-fourth Session of the Codex Committee on Food Additives and Contaminants (Unpublished FAO document, ALINORM 93/12; available from FAO or WHO). The Committee was also requested to comment on the safety of sodium iron EDTA as a dietary supplement for use in supervised food fortification programmes in populations in which iron deficiency anaemia is endemic.

The report of the meeting will appear in the WHO Technical Report Series. Its presentation will be similar to that of previous reports, namely, general considerations, comments on specific substances, and recommendations for future work. An annex will include a detailed table (similar to Table 1 in this report) summarizing the main conclusions reached by the Committee in terms of acceptable daily intakes (ADIs) and other toxicological recommendations. Information on specifications for the identity and purity of certain food additives examined by the Committee will also be included.

Toxicological monographs or monograph addenda on most of the substances that were considered will be published in WHO Food Additives Series, No. 32.

Specifications for the identity and purity of the compounds listed in Table 1 marked as N; N,T; R; or R,T will be published in the FAO Food and Nutrition Paper Series. Specifications for substances marked as S and S,T have been published previously in that series.

Table 1

ACCEPTABLE DAILY INTAKES, OTHER TOXICOLOGICAL INFORMATION, AND INFORMATION ON SPECIFICATIONS

Substance	Specifications[1]	Acceptable Daily Intake (ADI) in mg/kg of body weight and other toxicological recommendations
Antioxidants		
Dodecyl gallate	R	0 - 0.05 (temporary)[2]
Octyl gallate	R	0 - 0.1 (temporary)[2]
Propyl gallate	R	0 - 1.4
Flavouring agents		
Benzyl acetate	S	0 - 5 (group ADI)[2,3]
2-Ethyl-1-hexanol	N	0 - 0.5
d-Limonene	R	Not specified[4]
α-Methylbenzyl alcohol	N	0 - 0.1
Quinine hydrochloride	R }	Current use levels up to 100 mg/l (as quinine base) in soft drinks not of toxicological concern
Quinine sulfate	R }	
Flavour enhancers		
5'-Disodium guanylate	R }	Not specified[4]
5'-Disodium inosinate	R }	
Food colours		
Carotenes (algae)	R	No ADI allocated because the data were inadequate
Carotenes (vegetable)	R	Acceptable, provided the level of use does not exceed the level normally found in vegetables
Sweetening agents		
Maltitol	S }	Not specified[4]
Maltitol syrup	R }	
Saccharin	S	0 - 5
Thickening agents		
Konjac flour	N,T[2]	Not specified (temporary)[2,4]
Processed *Eucheuma* seaweed	R	0 - 20 (temporary)[2]
Propylene glycol alginate	R,T[2]	0 - 70
Miscellaneous substances		
ß-Cyclodextrin	N,T[2]	0 - 6 (temporary)[2]
Sodium iron EDTA	N,T[2]	Provisionally considered to be safe in food fortification programmes[5]
Sucrose acetate isobutyrate	R	0 - 10 (temporary)[2]
Urea	N	Use at levels up to 3% in chewing gum not of toxicological concern

Contaminant	Provisional Tolerable Weekly Intake (PTWI)
Cadmium	7 μg per kg of body weight
Chloropropanols (3-chloro-1,2-propanediol and 1,3-dichloro-2-propanol)	Levels in hydrolyzed vegetable proteins should be the lowest technologically achievable
Lead	25 μg per kg of body weight

Specifications only

Substance	Specifications[1]
Alginic acid	R
Ammonium alginate	R
Ammonium polyphosphate	R
α-Amylase from *Bacillus stearothermophilus*	R
α-Amylase from *Bacillus subtilis*	R
α-Amylase and glucoamylase from *Aspergillus oryzae*	R,T[2]
Calcium alginate	R
Carmines	R
Cochineal extract	R
Disodium pyrophosphate	R
Erythrosine	R
Ethyl hydroxyethyl cellulose	S,T[2]
ß-Glucanase from *Aspergillus niger*, var.	R
Hexane	S,T[2]
Lecithin	R
Lecithin, partially hydrolyzed	S
2-Nitropropane	S,T[2]
Oxystearin	S,T[2]
Petroleum jelly	S,T[2]
Potassium alginate	R
Sodium alginate	R
Sucralose (formerly trichlorogalactosucrose)	R
Tetrasodium pyrophosphate	R
Trichloroethylene	S,T[2]
Xanthan gum	R

Notes to Table 1

1. N, new specifications were prepared; R, existing specifications revised; S, specifications exist, revision not considered or not required; and T, the existing, new, or revised specifications are tentative and comments are invited.

2. See Table 2.

3. Group ADI with benzyl alcohol, benzaldehyde, benzoic acid, and benzoate salts.

4. ADI "not specified" means that, on the basis of the available data (chemical, biochemical, toxicological, and other), the total daily intake of the substance arising from its use at the levels necessary to achieve the desired effect and from its acceptable background in food does not, in the opinion of the Committee, represent a hazard to health. For that reason, and for the reasons stated in the individual evaluations, the establishment of an ADI expressed in numerical form was not deemed necessary.

5. The Committee provisionally concluded that sodium iron EDTA (ethylenediaminetetraacetate) meeting the tentative specifications prepared at the meeting does not present a safety problem when used in supervised food fortification programmes in iron deficient populations.

TABLE 2

FURTHER TOXICOLOGICAL STUDIES AND OTHER INFORMATION REQUIRED OR DESIRED

ANTIOXIDANTS

Dodecyl and octyl gallate

Additional information on the pharmacokinetic and metabolic behaviour of the gallates to help explain the differences in toxicological potency of the different gallate esters is required for review by 1996.

FLAVOURING AGENTS

Benzyl acetate

The Committee recommended that a full review of the group of compounds related to benzyl acetate, including benzyl alcohol, benzaldehyde, benzoic acid, and benzoate salts, should be performed in 1995.

THICKENING AGENTS

Konjac flour

The results of studies in rats and dogs known to have been completed and information on the fate of konjac flour in the gut are required for review in 1996.

Information is required on the level of lead in konjac flour.

Processed *Eucheuma* seaweed

Additional data known to exist on the characterization of the substance and complete details of the recent 90-day study in rats that was submitted for review, including individual animal histopathology data, are required for review in 1995.

Propylene glycol alginate

Information is required on the value of the actual average molecular weight, on the method of assay, on sample drying prior to analysis of total propylene glycol, and on the method and determination of total and free propylene glycol content.

MISCELLANEOUS SUBSTANCES

ß-Cyclodextrin

The results of a one-year study in dogs that is known to be underway and information on the effects of ß-cyclodextrin on the availability of lipophilic nutrients are required for review in 1995.

Information is required on:

1. the range of production methods used;
2. the levels of other cyclodextrins in commercial products;
3. solvents used in manufacture, residual levels of solvents, and methods of analysis; and
4. information on the source and availability of α-, ß-, and γ-cyclodextrins and their characterization.

Sodium iron EDTA

Information is required on the food-grade material and on the methodology for nitrilotriacetic acid.

Sucrose acetate isobutyrate

Information to clarify the effects of this substance on hepatobiliary function in the dog compared with other species, in particular the human, is required by 1996.

FOOD ADDITIVES FOR SPECIFICATIONS ONLY

α-Amylase and glucoamylase from *Aspergillus oryzae*

Information is required on the levels and methods of analysis for α-cyclopiazonic acid and kojic acid.

Ethyl hydroxyethyl cellulose

Information is required on methods of analysis and limits for ethylene oxides and, where applicable, for ethylene glycols, 1,4-dioxane, and ethylene chlorohydrin.

Hexane

Information is required on limits for aromatic hydrocarbons

2-Nitropropane

Information is required on the refractive index range applicable to commercial products and on the adequacy of the method of assay.

Oxystearin

Information is required on the methods of analysis for epoxides.

Petroleum Jelly

Information is required on the actual composition of hydrocarbons, the methods for identification of individual hydrocarbons, limits and methods of analysis for sulfur, arsenic, lead, and heavy metals, as well as on the nature of the sulfur compounds.

NOTE

This document has been distributed prior to publication of the full report of the forty-rst meeting of the Joint FAO/WHO Expert Committee on food Additives (JECFA) to nsure the fast dissemination of information, in particular to the Codex Alimentarius :ommission, to which JECFA is the scientific advisory body on matters relating to food dditives and contaminants.

The FAO and WHO Joint Secretaries of JECFA request that further inquiries regarding ıe compounds evaluated at the forty-first meeting of the Committee be made only after the ıll official report has been published and distributed by WHO in the name of both ponsoring Organizations, FAO and WHO. Your cooperation is very much appreciated.

= = =

Appendix 18

Effectiveness of Iron-Fortified Infant Cereal in Prevention of Iron Deficiency Anemia

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ABSTRACT. *Background.* Iron deficiency continues to be a common problem among infants throughout the world. Iron-fortified formula is effective in preventing iron deficiency but the benefit of iron-fortified cereal is controversial.

Methods. We compared iron-fortified rice cereal to unfortified rice cereal in infants who were exclusively breast-fed for more than 4 months and to iron-fortified formula in infants who were weaned to formula before 4 months of age. The design was double blind in respect to the presence or absence of fortification iron in the cereal or formula and included 515 infants who were followed on the protocol from 4 to 15 months of age. Rice cereal was fortified with 55 mg of electrolytic iron per 100 g of dry cereal and infant formula with 12 mg of ferrous sulfate per 100 g of dry powder, levels approximating those in use in the United States. Measures of iron status were obtained at 9, 12, and 15 months. Infants with hemoglobin levels of <105 g/L were excluded from the study and treated.

Results. Consumption of cereal reached plateaus at means of about 30 g/d after 6 months of age in the formula-fed groups and 26 g/d after 9 months in the breast-fed groups; these amounts are higher than the 19-g/d mean intake by the 73% of infants who consume such cereal in the United States. Among infants weaned to formula before 4 months, the cumulative percentages of infants excluded for anemia by 15 months were 8%, 24%, and 4%, respectively, in the fortified cereal, unfortified cereal and formula, and fortified formula groups ($P < .01$ unfortified vs either fortified group; the difference between the two fortified groups was not significant). In infants breast-fed for more than 4 months, the corresponding values were 13% and 27%, respectively, in the fortified and unfortified cereal groups ($P < .05$). Mean hemoglobin level and other iron status measures were in accord with these findings.

Conclusion. Iron-fortified infant rice cereal can contribute substantially to preventing iron deficiency anemia. *Pediatrics* 1993;91:976–982; *iron deficiency, anemia, infant, cereal.*

ABBREVIATION. INTA, Institute of Nutrition and Food Technology.

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There is substantial evidence that iron-fortified infant formula is a reliable means of preventing iron deficiency anemia. In contrast, as was recently pointed out by Fomon,[1] there has been relatively little evidence that infant cereal plays a similarly useful role. He concluded that "at present, the major reason for recommending iron-fortified infant cereal appears to be long-established tradition." The most optimistic data in regard to the effectiveness of cereal as a vehicle for fortification iron were the studies of Rios and coworkers.[2] Iron 59 was used as an extrinsic label to estimate the absorption of fortification iron from rice cereal and infant formula. Absorption of electrolytic iron from cereal was about 4%, roughly the same percentage as from the ferrous sulfate iron that was used to fortify infant formula. However, there was some doubt about the applicability of these results to the infant cereals that are most widely used in the United States because of differences in particle size of the electrolytic iron.[1] The electrolytic iron used in the absorption studies had a smaller particle size distribution than the electrolytic iron routinely used to fortify infant cereal. Since iron of smaller particle size is better absorbed than larger particles, it is possible that iron was better absorbed in the tracer studies than it would be from commercially available iron-fortified infant cereal.

In accord with this interpretation, many subsequent studies of absorption of labeled iron from infant cereals, mostly done in adults, showed that only a very low percentage was absorbed.[3] The addition of ascorbic acid could enhance the absorption of iron. But the lability of ascorbic acid during processing and storage remains a problem. Most importantly, any estimate of effectiveness of fortified cereal in preventing iron deficiency anemia has been based primarily on extrapolation from absorption data. The sort of carefully monitored field trials that have helped to establish the efficacy of iron-fortified infant formula[4–6] have not been performed with iron-fortified cereal.

The generally skeptical and pessimistic view that iron is poorly absorbed not only from cereal but also from legume products may not be justified. Of special interest in this regard is the study of the effect of soy-based formula on iron nutrition in infants from the Institute of Nutrition and Food Technology (INTA), Universidad de Chile, Santiago.[7] Despite extremely poor bioavailability from extrinsically labeled iron when measured in adults, iron-fortified

soy formula proved to be essentially as effective as iron-fortified cow milk formula in preventing iron deficiency anemia when it was fed to infants during their first year. When there is a such striking discrepancy between an extrapolation and the actual clear-cut prevention of iron deficiency anemia under conditions of normal feeding, the latter carries far more credibility. An infant feeding trial would therefore be a useful means of establishing the effectiveness of iron-fortified infant cereal in preventing iron deficiency anemia.

The purpose of this study was to determine the effectiveness of a dry rice cereal as it is currently fortified and marketed in the United States in preventing iron deficiency anemia in infants when used under optimal conditions. The results are based on 515 healthy infants who weighed more than 3000 g at birth and who were fed cereal starting at 4 months of age. Under the conditions used, an average of 25 to 30 g of infant cereal consumed per day proved to be a useful means of preventing iron deficiency anemia.

MATERIALS AND METHODS

The infant cereal used in this study was the dry infant rice cereal manufactured by Gerber Products Company (Fremont, MI). The cereal was provided in two forms. The first was fortified with electrolytic iron to a level of 35 mg/100 g dry cereal, the same as in the commercial product. Note that the actual content of iron in cereal is usually somewhat higher than the label claim amount of 45 mg/100 g to meet the Food and Drug Administration requirement that the content be as least as high as claimed on the label. The second form of cereal was identical with the first except that fortification iron was omitted.

Infant formula for the study was formulated by INTA, Chile, in iron-fortified and iron-unfortified forms.[7] The fortified product contained added ferrous sulfate to supply 12 mg of iron per reconstituted liter. The unfortified product contained no added iron. Both products were supplemented with other minerals and vitamins, corresponding to the composition of currently marketed products in Chile and in accord with the US Infant Formula Act of 1985.[10] The formula contained added ascorbic acid, 66 mg per reconstituted liter.

Study Design

The population of infants was from a low and low-middle income group living in urban Santiago, Chile, and receiving their routine pediatric care in a Ministry of Health outpatient clinic. All infants weighed more than 3000 g at birth and had no serious medical problems. Other criteria for initial inclusion in the study were presence of a consistent caretaker and history of having received no iron-fortified formula or supplemental iron in the past. All mothers were literate and capable of keeping records of food consumptions and morbidity. Infants whose hemoglobin concentration was less than 95 g/L at 4 months of age were not included in the study. The assignment to groups was based first on whether the period of exclusive breast-feeding was less or greater than 4 months. Infants who were weaned to formula before 4 months of age were randomized to three groups as shown in Fig. 1. Weaning was defined as more than 50% of estimated caloric requirements coming from a source other than breast milk. Group 1 received iron-fortified cereal but unfortified formula and can be considered the cereal test group. Group 2 received unfortified cereal and unfortified formula, in accord with current nutrition management in Chilean Ministry of Health clinics. On similar regimens, the experience has been that about 20% of infants will have developed mild iron deficiency anemia at 12 months of age.[8] Group 3 received unfortified cereal and iron-fortified formula. In this setting, a milk formula fortified with similar levels of iron and ascorbic acid resulted in only 1% having iron deficiency anemia at 12 months of age.[8]

Infants who were still exclusively breast-fed at 4 months of age were randomized to two groups. Group 4 received the iron-fortified cereal and group 5, the unfortified cereal. When infants were subsequently weaned at some time after 4 months of age, the unfortified formula was supplied. Solid foods were recommended for all babies according to the usual practice in Chile: fruits and juices starting at 3 months, vegetables and meat at 4 months, legumes at 6 months, and regular "table" food at 9 months.

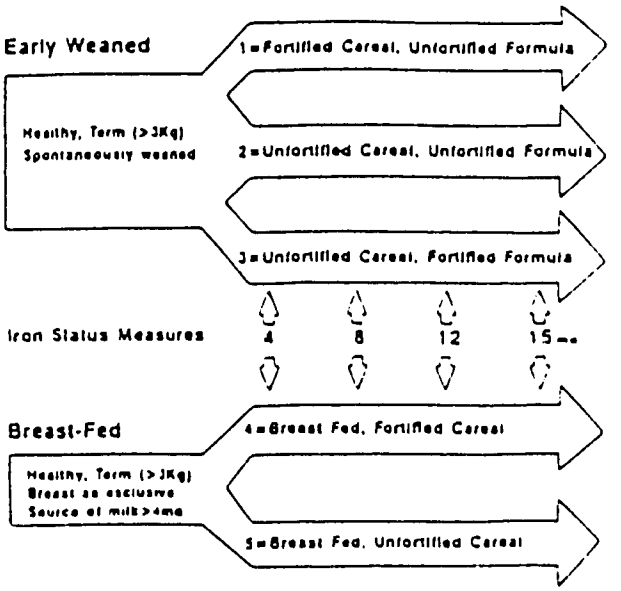

Fig 1. A schematic representation of the experimental design. Included are three groups of formula-fed infants (groups 1 through 3) and two groups of breast-fed infants (groups 4 and 5).

The five groups were similar in birth weight, sex ratio, growth pattern, and socioeconomic level. The other solid foods used were not iron-fortified and there was little meat in the diet. Once enrolled in the study, the most common reasons for failure to complete the protocol were a move of the household to another area (6.8%) and failure to comply with the feeding regimen or with record keeping of food consumption and morbidity (5.6%). The total percentage of infants excluded was 20.6%.

Procedures

Pediatricians participating in the study performed monthly clinical and anthropometric evaluations from 4 to 15 months of age; in addition, they provided routine health maintenance and sick visit care. Morbidity since the previous visit was also recorded. A registered field dietitian performed weekly home visits during this period to instruct mothers on feeding, well-baby care, and the daily recording of formula consumption and illnesses or symptoms. Formula and cereal intake were estimated by the mother, who was given a measuring spoon for preparing cereal and formula from the dry forms in which they were supplied. All formulas were provided at no charge. Initial hemoglobin screening for inclusion in the study was by capillary heel-stick (HemoCue, Leo Diagnostics, Helsingborg, Sweden). Iron nutritional status was subsequently determined from venous blood at 8, 12, and 15 months of age. The following were measured as previously described[8]: hemoglobin, mean corpuscular volume (Coulter model ZBI, Hialeah, FL), iron concentration and iron-binding capacity, erythrocyte protoporphyrin (Hematofluorometer AVIV, Lakewood, NY), and serum ferritin (Ferrizyme, Abbott Diagnostics, North Chicago, IL). Serum ferritin values for infants receiving iron-fortified formula were lower than historical control values from INTA. However, they were carefully verified by reassay against an international standard and previous samples.

Mean, standard deviation, Student's t test, and χ^2 were used in the statistical analysis. Questions about differences between groups that were generated by our hypotheses generally involved comparing two groups: fortified cereal vs unfortified cereal, fortified cereal vs fortified formula, breast-fed + fortified cereal vs breast-fed + unfortified cereal.

The protocol was approved by the Ethics Committee for Human Research of the INTA. Informed consent was obtained verbally from parents prior to inclusion in the study.

RESULTS

Growth, Morbidity, and Attrition

Weight and length at 8, 12, and 15 months were essentially the same in the three formula-fed and two breast-fed groups, respectively. Only at 8 months of age were the breast-fed infants very slightly but significantly heavier than the formula-fed infants ($P < .001$) (Fig. 2). At each age, both breast-fed and formula-fed groups had mean weights just above the 50th percentiles of US standards.[11] Morbidity was expressed as number of clinic outpatient visits per year per infant and consisted primarily of respiratory infections (mean: 2.54 visits) and diarrhea (mean: 0.51 visits). There were no significant differences in morbidity as a function of iron fortification or breast-feeding vs formula-feeding. There were essentially no differences among groups in the percentage of infants who dropped out of the study for reasons other than the development of anemia.

Cereal Consumption

Mean cereal consumption in all three formula-fed groups (groups 1 through 3) closely approached the target level of 30 g/d within 3 weeks of initiation of cereal at 4 months of age (Fig. 3). Cereal consumption was then maintained at that level for the entire period of the study, to 15 months of age. Fewer than 20% of infants failed to maintain their cereal consumption above 24 g/d.

The two breast-fed groups (groups 4 and 5) were slower to reach target levels of cereal consumption and reached a slightly lower plateau of mean intake than the formula-fed infants (fig. 3). The mean intake reached 20 g at 6 months and 25 g at about 7.5 months. This was despite the encouragement of cereal consumption by the nutritionists on the weekly home visits and may be attributable to the difference in ease of feeding cereal mixed with formula and fed from the bottle compared to feeding it with a spoon as a gruel.

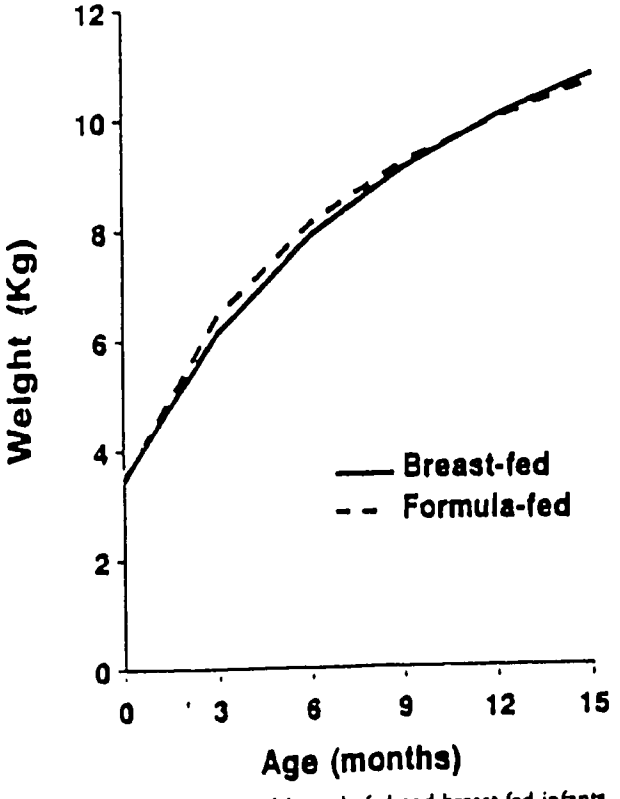

Fig 2. Mean weight gain of formula-fed and breast-fed infants.

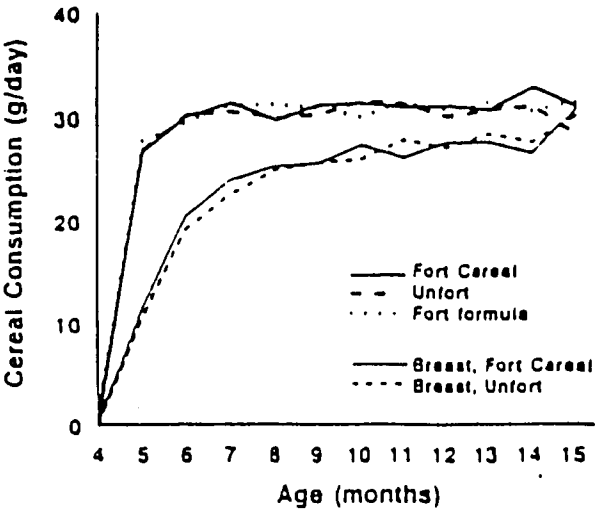

Fig 3. Cereal consumption of formula-fed and breast-fed infants. The breast-fed infants were slower to increase their cereal consumption and did not reach as high an intake as the formula-fed infants.

Infants in groups 4 and 5 remained breast-fed for a relatively long time, about half still being exclusively breast-fed at 8 months of age. They were categorized as formula-fed even if they received as little as one bottle per day. Cereal consumption was slightly higher in infants who were weaned to formula than among those who continued exclusively breast-feeding. The difference was calculated for each month and was about 1 g/d in group 4 and 1 to 4 g/d in group 5 between 6 and 12 months of age; the difference was not statistically significant except at 8 months in group 5 ($P < .05$).

Formula-Fed Infants

The Table summarizes the laboratory data at 8, 12, and 15 months of age. Group 1 infants who received fortified cereal but unfortified formula had significantly higher hemoglobin values ($P < .01$) at all three ages compared to group 2 infants, who received no fortified foods. There were no significant differences in hemoglobin concentration between group 1 (fortified cereal) and group 3 (fortified formula). However, mean values for mean corpuscular volume, and transferrin saturation were higher and erythrocyte protoporphyrin was lower in group 3. Among the breast-fed infants, the hemoglobin concentration was significantly higher ($P < .05$) at 12 and 15 months in group 4, which received iron-fortified cereal, compared with group 5, which received unfortified cereal.

Figure 4 shows the cumulative percentage of infants who were excluded from the protocol because they had a hemoglobin concentration of less than 105 g/L. Group 3, fed iron-fortified formula, maintained a plateau of about 3% after 8 months of age, in accord with previous studies from INTA. Group 1, fed iron-

TABLE. Laboratory Data*

Age mo	Groups	n	Hb, g/L	Hb < 105, %	MCV, fL	EP, µg/dL RBC	SAT, %	SF,† µg/L
8	1. Fortified cereal, unfortified formula	84	118 ± 1.0	6.0	73.9 ± 0.4	128 ± 6	11.7 ± 0.7	10 (5–2
	2. Unfortified cereal, unfortified formula	93	114 ± 1.5	12.9	72.0 ± 0.4	136 ± 5	10.0 ± 0.6	8 (3–
	3. Unfortified cereal, fortified formula	94	121 ± 0.9	3.2	77.3 ± 0.4	120 ± 5	13.1 ± 0.7	10 (5–
	4. Fortified cereal, breast-fed	85	116 ± 0.9	10.6	73.0 ± 0.5	103 ± 3	11.3 ± 0.6	16 (7–3
	5. Unfortified cereal, breast-fed	88	114 ± 1.0	14.8	73.7 ± 0.5	127 ± 7	10.0 ± 0.6	13 (6–32
12	1. Fortified cereal, unfortified formula	71	124 ± 1.0	2.8	73.4 ± 0.4	107 ± 3	13.5 ± 0.8	9 (4–18
	2. Unfortified cereal, unfortified formula	74	120 ± 1.0	8.1	73.2 ± 0.6	130 ± 7	11.7 ± 0.9	7 (3–15
	3. Unfortified cereal, fortified formula	77	125 ± 0.9	0.0	76.1 ± 0.4	95 ± 3	15.4 ± 0.8	11 (6–20
	4. Fortified cereal, breast-fed	74	121 ± 0.9	1.4	75.1 ± 0.4	110 ± 7	12.9 ± 0.8	15 (7–30
	5. Unfortified cereal, breast-fed	74	117 ± 1.0	10.8	72.5 ± 0.5	129 ± 7	11.6 ± 0.8	10 (4–24
15	1. Fortified cereal, unfortified formula	67	126 ± 1.1	0.0	76.3 ± 0.4	100 ± 4	15.0 ± 1.0	10 (5–21
	2. Unfortified cereal, unfortified formula	64	121 ± 1.6	9.1	74.3 ± 0.6	116 ± 6	11.8 ± 0.8	8 (4–16
	3. Unfortified cereal, fortified formula	73	126 ± 1.0	1.4	76.4 ± 0.4	95 ± 3	15.8 ± 0.9	11 (5–22
	4. Fortified cereal, breast-fed	72	124 ± 1.0	1.4	76.3 ± 0.5	105 ± 6	14.7 ± 1.0	11 (6–21
	5. Unfortified cereal, breast-fed	64	119 ± 1.0	3.2	75.3 ± 0.5	118 ± 6	13.4 ± 0.9	10 (5–21

* Mean and SEM are indicated. Difference in Hb between groups: 1 vs 2, $P < .01$ at all ages; 1 vs 3: not significant at all ages; 4 vs 5: $P <$ .05 at 12 and 15 months. Abbreviations: Hb, hemoglobin; MCV, mean corpuscular volume; EP, erythrocyte protoporphyrin; RBC, red blood cells; SAT, transferrin saturation; SF, serum ferritin.
† Geometric mean ± 1 SD range.

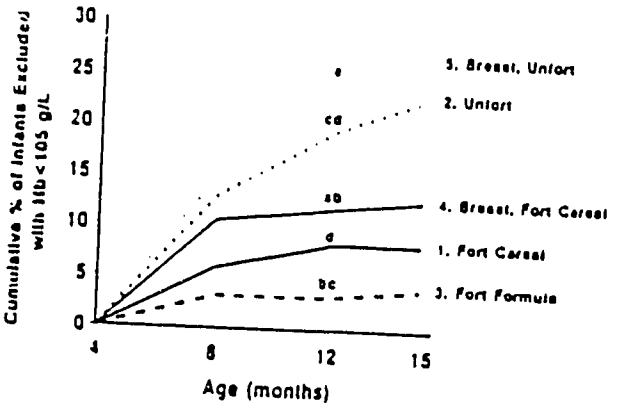

Fig 4. Cumulative percentage of infants excluded from the regimen on the basis of a concentration of hemoglobin (Hb) <105 g/L. At 12 months of age, fewer formula-fed infants had been excluded if they had received either fortified cereal (Fort Cereal) or formula (Fort Formula) than if they had received neither food in the fortified form (Unfort). Fewer breast-fed infants had been excluded from the fortified cereal group (Fort Cereal) than from the unfortified cereal group. Infants fed iron-fortified formula were less frequently excluded than breast-fed infants fed iron-fortified cereal.

fortified cereal, had a cumulative exclusion rate of 6% at 8 months, leveling off at 8% at 12 and 15 months. In marked contrast, group 2, which had received no fortified food, had 13% excluded at 8 months, and increasing cumulative totals of 19% at 12 months and 24% at 15 months of age, respectively. Chi-square analyses for differences in exclusion rates between groups were done at 12 months, a common time for anemia screening in practice and a period where study infants had been on the dietary regimens for 8 months. Each formula-fed group receiving some form of fortification (group 1 or 3) was significantly less likely than unfortified group 2 to have a hemoglobin concentration of less than 105 g/L ($P < .05$ for 1 vs 2 and $P < .001$ for 2 vs 3). Although the values suggested a slight advantage of group 3 over group 1, the difference between the two groups was not statistically significant.

Figure 5 compares the groups in respect to the laboratory measurements of iron status at 8 months of age, before any infants had been excluded for anemia. The height of the bars represents the percentage of infants with iron deficiency anemia in each diet group. Iron deficiency anemia was defined essentially as previously,[3] as a hemoglobin concentration of less than 110 g/L in combination with two or three additional abnormal iron status measures out of 3 (mean corpuscular volume <70 fl, SAT <10%, and serum ferritin <10 µg/L). These results parallel those depicted in Fig. 4, but are more specific to iron deficiency as a cause of anemia. In groups 1 and 3, 6% and 4%, respectively, had iron deficiency anemia, significantly fewer than the 17% in group 2 (both $P < .05$ by χ^2).

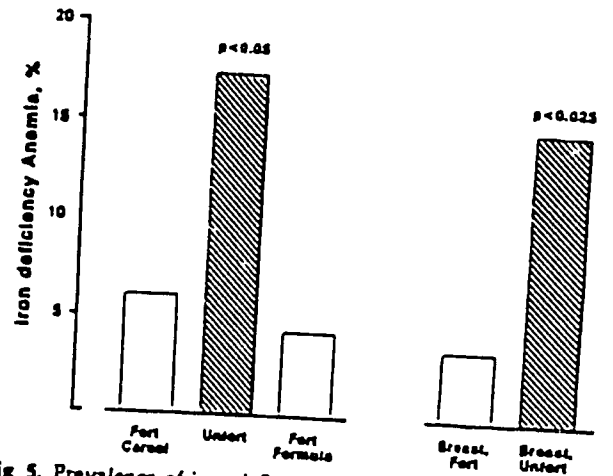

Fig 5. Prevalence of iron deficiency anemia at 8 months of age. Among the formula-fed infants, groups 1 and 3, who received iron-fortified cereal (Fort Cereal) and iron-fortified formula (Fort Formula), respectively, had a significantly lower prevalence of anemia than the group 2 infants, who received neither fortified cereal nor formula (Unfort). Breast-fed infants receiving iron-fortified cereal (Breast, Fort) had a significantly lower prevalence of iron deficiency anemia than those who received unfortified cereal (Breast, Unfort).

Breast-Fed Infants

Infants who were breast-fed more than 4 months and who were fed iron-fortified cereal (group 4) had a significantly higher ($P < .05$) mean hemoglobin concentration than unfortified cereal group 5 infants at 12 and 15 months of age (Table). The cumulative percentage of group 4 infants excluded from the protocol on the basis of a hemoglobin concentration of less than 105 g/L reached a value of 11% at 8 months of age and scarcely rose above that level subsequently (Fig. 4). In contrast, the corresponding percentage in group 5 continued to increase from 15% at 8 months to 24% at 12 and 27% at 15 months of age. At 12 months of age, group 4 had had significantly fewer individuals excluded for a hemoglobin concentration of less than 105 g/L than group 5 ($P < .025$). Figure 5 shows that the percentage with iron deficiency anemia in group 4 was a surprisingly low 3%, in the same low range as in the two formula-fed groups that received some form of iron fortification, either from cereal or from formula. However, 15% of the breast-fed infants receiving unfortified cereal had developed iron deficiency anemia, a significantly higher percentage than in group 4 ($P < .01$).

DISCUSSION

There is now virtual agreement about the guidelines for infant feeding in the United States.[12] The promotion of breast-feeding is universally supported, and iron-fortified formula rather than cow milk or unfortified formula is recommended at weaning if, as is the case with most infants, weaning occurs before 12 months of age. One issue that has remained unresolved is the efficacy of iron-fortified infant cereal as an alternative source of fortification iron.[1] Infant cereal is the most commonly used first nonmilk food in the infant diet, and it is recommended as a source of iron for late infancy,[13] when the risk of iron deficiency is greatest and milk should no longer be the sole source of calories.

Under the conditions of this study, infant cereal fortified with electrolytic iron in the same way as in the United States was quite effective in preventing iron deficiency anemia when it was the only iron-fortified product used. It is worth emphasizing that all infants whose hemoglobin concentration fell below 105 g/L were taken out of the study and given iron. Had this not been the case, the differences between the iron-supplemented and unsupplemented groups would probably have been substantially greater. For this reason, Fig. 5, giving the prevalence of anemia at 8 months, and Fig. 4, showing the cumulative percent of infants excluded from each group, best depict the benefits of iron fortification. In contrast, in the Table the differences between groups at 12 and 15 months may at first seem less impressive, presumably because the most iron-deficient infants have been excluded. Consequently, those remaining in the study were infants who were most resistant to iron deficiency, perhaps through individual variations such as higher neonatal iron stores. The Table suggests that iron-fortified formula had a modest though not statistically significant advantage over iron-fortified cereal at 8 months.

Figure 4 shows the *cumulative* percentage of infants in each group who were excluded on the basis of a hemoglobin concentration below 105 g/L. Since values below 105 g/L have been associated with impaired psychomotor development, these are the infants about whom there is concern in regard to the physiological consequences of iron deficiency.[14,15] As shown in Fig. 4, all three groups that received either iron-fortified cereal or formula had a clear advantage over the other two groups (upper curves) that were given no iron-fortified foods. It is noteworthy that individuals in groups 1, 3, and 4 were most likely to become anemic at 8 months of age and showed relatively little increase subsequently, after these most anemic infants had been removed from the study for iron treatment. In contrast, groups 2 and 5 (no fortification) showed a steadily increasing percentage that developed anemia (hemoglobin <105 g/L). Group 3 (iron-fortified formula) had the fewest infants with a hemoglobin level of less than 105 g/L, about 3%. Group 1 (iron-fortified cereal) reached slightly higher values for prevalence of anemia of 6% at 8 months and 9% at 12 and 15 months, but there was no statistically significant difference with group 3. However, group 2, which had received no iron-fortified food, steadily diverged from these results, with 20% who were anemic (hemoglobin <105 g/L) at 12 months and 22% at 15 months.

The next issue to address is how well the cereal results in Chile reflect conditions in the United States. In the broadest terms, although the study population is less well off economically than a comparable US population, the advantages of excellent pediatric care and access to ample food, electricity, and running water help to explain why anthropometric[11] and morbidity data do not differ substantially from the United States. Two factors that probably promoted the effectiveness of iron-fortified cereal in Chile were the relatively high consumption of cereal and the fact that it was fed, as is customary in Chile, mixed with a formula that was fortified with ascorbic acid, a known enhancer of iron absorption. A recent survey in the United States showed that the average consumption of infant cereal between 6 and 12 months of age was 19 g/d among the 73% of infants who consumed cereal.[16] However, iron-fortified cereal in the United States is probably fed with a more ascorbic acid-rich diet. Furthermore, even "unfortified" US formulas comply with the Infant Formula Act of 1985 by adding iron to a concentration of at least 1.0 mg/L,[9] an amount that is considerably higher than that of the INTA formula in this study, which contained about 0.5 mg of endogenous iron per liter. The INTA formula is similar in iron content to that used in the distribution program of the Chilean Ministry of Health.

Iron-Fortified Cereal in Breast-Fed Infants

Infants who were breast-fed for 4 or more months also showed marked benefit from receiving iron-fortified cereal. In these infants, cereal was fed by spoon, as in the United States until weaning to the bottle, when it was added to the formula in the manner that is customary in Chile. The Table shows that hemo-

globin and other measures of iron nutrition were indicative of significantly better iron status in fortified group 4 compared to unfortified group 5, especially at 12 and 15 months of age, by which time cereal had been consumed for a more prolonged period. Figure 4 shows the differences even more clearly. By 15 months of age, hemoglobin had fallen below 105 g/L in 27% of infants in group 5 compared to 12% in group 4.

It is also worth comparing breast-fed, fortified-cereal group 4 with the fortified formula-fed group 3. Although the concentration of hemoglobin in group 4 was lower at 8 months (Table), when the breast-fed infants had had a relatively brief exposure to the fortified cereal, the difference, though significant ($P < .05$), diminished by 12 and 15 months of age.

The results for the breast-fed infants are in accord with other recent studies showing that there is a substantial risk of iron deficiency anemia after about 6 months of age unless a source extra iron is provided.[9-12] This may be attributed to an exhaustion of storage iron during rapid growth[13] and, to a lesser degree, a declining concentration of iron in breast milk.[14] It is possible that the provision of iron-fortified cereal to breast-fed infants in the United States provides better protection against iron deficiency than in this study since sources of ascorbic acid, such as fruit and fruit juices, are more often fed with cereal and would further enhance the absorption of fortification iron. Furthermore, when infants are weaned, they are given iron-fortified formula according to present recommendations. In contrast, the Chilean infants are weaned to a formula that contains less iron than provided by "unfortified" formula in the United States. However, the current pattern of cereal consumption in the United States is more variable and, on the average, less is consumed per day than in this study.[16]

Role of Cereal as a Vehicle for Iron Fortification

Infant cereal was first fortified in the United States in 1940s and 1950s, shortly after World War II. Initially cereal was fortified with iron pyrophosphate or orthophosphate, compounds that allowed for a prolonged shelf-life but that subsequently proved to be poor sources of absorbable iron. Since 1972, electrolytic iron has been most widely used in the fortification of infant cereal in the United States,[3] currently at a label claim level of 45 mg/100 g dry cereal. However, the effectiveness of infant cereal as a vehicle for fortification iron has not become as well established as is the case with infant formula.

Tracer studies of electrolytic iron absorption from cereal were initially encouraging,[2] but the particle size of the fortificant studied differed from that in commercial use and made it difficult to extrapolate to infants eating the marketed products.[1] In the meantime, iron-fortification of formula proved to be effective in preventing iron deficiency in infants, and recommendations for infant feeding increasingly reflected a sole reliance on infant formulas for this purpose.[18]

It may at first seem unnecessary to have a continuing interest in infant cereal as a vehicle for fortification iron for infants. The biggest disadvantage of infant cereal as the sole source of iron is that the amount that is consumed varies considerably from infant to infant. Of course, the same is true of the long-accepted iron fortification of cereal and flour products consumed by the general population. However, in infants, the issue is of more critical importance because iron deficiency anemia is associated with a delay in psychomotor development that may be long-lasting and not completely reversible, even when the deficiency is reversed.[14,15] The problem of inconsistent cereal consumption could probably be alleviated if it were routinely dealt with as a part of nutrition counseling during a health maintenance visit.

There are several reasons to give infant cereal continued attention as a vehicle for fortification iron. First, cereal products are relatively inexpensive and quite stable on storage even after the package has been opened. Low cost is an important factor in the planning of public assistance programs such as the Women, Infants, and Children (WIC) program in the United States. It is also a factor in infant feeding programs internationally, and the Agency for International Development continues to distribute cereal and legume products fortified with iron and ascorbic acid on a large scale to developing countries.[21] Another reason that cereal is an attractive vehicle is that it is traditionally among the most important weaning foods in the United States and in many countries around the world. It is therefore consumed during a period when iron deficiency is most common. It is also a food that helps to make the transition out of the physiologically high fat diet that is exemplified by breast milk and that is necessary for rapid infant growth. A diet higher in carbohydrate is more appropriate for the slower growth of childhood and is currently recommended for this group.

CONCLUSION

Iron-fortified dry infant cereal plays a meaningful role in the prevention of iron deficiency anemia in infancy.

ACKNOWLEDGMENT

This work was supported by grants from Nutrition Foundation, Inc. subdivision of International Life Sciences Institute, Human Nutrition Institute.

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COMORBIDITY BETWEEN ADDH AND LEARNING DISABILITY: A REVIEW AND REPORT IN A CLINICALLY REFERRED SAMPLE

Garet Semrud-Clikeman, Ph.D., Joseph Biederman, M.D.,
Susan Sprich-Buckminster, B.A., Belinda Krifcher, B.A.,
Stephen V. Faraone, Ph.D., and Dennis Norman, Ed.D.

Abstract. A widely variable overlap ranging from 10 to 92% has been reported in the literature between attention deficit disorder with hyperactivity (ADDH) and learning disability (LD), most likely a result of inconsistencies in the criteria used to define LD in different studies. The following study seeks to more accurately determine rates of LD in clinically referred children. Using a psychometrically reliable approach, it was expected that the rate of LD in ADDH children would be far more modest than previously reported. Subjects were referred children with ADDH ($N = 60$), children with academic problems ($N = 30$), and normal controls ($N = 36$) of both sexes with available psychological and achievement testing. Using a liberal definition of LD, significant differences were found between the groups (ADDH = 38% versus academic problems = 43% versus normals = 8%; $p = 0.002$). In contrast, more modest rates were found using two more stringent methods of assessment (23 and 17%; 10 and 3%; 2 and 0%, respectively; $p = 0.02$). Arithmetic-based LD appears to be equally identified by both stringent methods, whereas the liberal definition overidentified children in all three groups. These findings show that a liberal definition of LD overidentifies LD not only in ADDH children but also in normal children. *J. Am. Acad. Child Adolesc. Psychiatry* 1992;31:439–448. Key Words: learning disability, attention deficit disorder, attention-deficit hyperactivity disorder, comorbidity.

Appendix 19

International Nutrition Planners Forum

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INPF Steering Committee

Appendix 20

INTERNATIONAL NUTRITION PLANNERS FORUM
STEERING COMMITTEE MEETING

Sunday, 7 March 1993
Novotel Mt. Meru Hotel
Arusha, Tanzania

MINUTES

I. Call to Order

The meeting was called to order by Dr. Mamdouh Gabr, Chairman, at 13:35 p.m. A list of those present is attached. Dr. Gabr introduced Dr. Samuel G. Kahn representing Mr. Richard Seifman and Ms. Catherine Siandwazi of the Commonwealth Regional Health Community Secretariat for East, Central and Southern Africa.

II. Approval of the Minutes of the 3 September 1991 Meeting

At the request of Dr. Jaime Ariza, the minutes were amended as follows: delete "working in Latin America" from bottom of page 4. The minutes were approved as amended.

III. Secretariat Update of INPF Activities Since the Last Steering Committee Meeting

Dr. Suzanne Harris, INPF Secretariat, reported that response to the publication of the Sixth INPF Conference summary was strong. Announcements of the publication's availability appeared in "Mothers and Children", a newsletter of the American Public Health Association, in the Journal of the American Dietetic Association, and in the Journal of Nutrition Education. Dr. Kahn shared copies of the Development Communication Report no. 79 published by USAID, which also advertized the summary's availability (page 22).

Dr. Harris reported that the French and Spanish translations of the summary are ready for printing. Dr. Ariza requested that copies in Spanish be distributed to a list of Latin American Schools of Public Health and Dietetics which he will provide. Dr. Gabr suggested that UNICEF might be willing to distribute copies. He also suggested sending copies to USAID missions. Dr. Harris reported that Cheryl Achterberg is now working with FAO on a nutrition education project.

Dr. Aree Valyasevi reported on his efforts to share the outcome of the Sixth INPF Conference with participants at the Sixth Asian Congress of Nutrition held in Kuala Lumpur, Malaysia in September 1991. There was a discussion of training needs for Asia with 20 individuals representing 12 countries. UNICEF (Bangkok office) will sponsor another workshop prior to the Seventh Asian Congress to be held in Peking in 1995.

Dr. Ariza shared the outcome of the Sixth INPF Conference at the Society of Latin American Nutritionist (SLAN) also held in September 1991. In addition to referencing the meeting in his remarks, he distributed copies of "Crucial Elements of Successful Community Nutrition Programs". He will send a list of Schools of Public Health and Dietetics to whom the Spanish version of the conference report should be distributed.

The Secretariat reported that the conference was discussed at the International Session during the annual meeting of the Society of Nutrition Education held in July 1992.

The Steering Committee encouraged the Secretariat to seek additional avenues for distributing the summary including distribution to the Nutrition Policy Board of the U.S. Department of Health and Human Services in Washington, DC.

The group discussed other ways of increasing the visibility of INPF including an informal meeting at the International Congress of Nutrition to be held next fall in Adelaide, Australia under the auspices of the International Union of Nutritional Scientists (IUNS) and the Australian Nutrition Society. The concept of social marketing is still controversial and Ms. Julia Tagwireyi pointed out the lack of trained communications personnel in many LDCs.

IV. Regional Nutrition Networks

As a result of conversations between Mr. Seifman, Dr. Gabr, Ms. Tagwireyi and Dr. Harris during the International Conference on Nutrition in Rome last December, Dr. Ariza, Dr. Wynette Patterson and Ms. Siandwazi were asked to describe the activities of the nutrition networks with which each works.

Dr. Ariza described RORIAM which roughly translates as the Latin American Institutional Network on Food and Nutrition started in 1984 by the Pan American Health Organization (PAHO). Its role is to coordinate and support nutrition activities within and between countries working with multi and bilateral organizations. RORIAM is involved in interdisciplinary research, manpower development, policy and planning, communication and integration of technical groups. It includes all of the Latin American nutrition institutes - Chile, INCAP, Uruguay, Mexico, Brazil, and the Caribbean. More recently Venezuela, Ecuador, Argentina, and Puerto Rico have joined. The U.S. Centers for Disease Control and the U.S. Department of Agriculture also participate.

Funds are always a problem. Last fall with a grant from the Kellogg Foundation, a meeting was organized in Guatemala for the purpose of profiling the prevalence of chronic noncommunicable diseases in Latin America. These data will be complied at the country level and utilized in policy development. FAO and PAHO have inexpensive software systems for handling such data. A preliminary report on these data is expected shortly and the final report, being developed by INCAP, should be published in early 1994.

Dr. Valyasevi reported that a similar network exists in Southeast Asia with meeting once or twice a year. They are focussing on standardizing methodologies with the help of the WHO office in Delhi.

Dr. Patterson described the Caribbean Food and Nutrition Institute (CFNI) begun 25 years ago with core funds from PAHO, WHO, and some national funds. The Institute is linked to the national Ministries of Health and Agriculture. They are now trying to develop links with Ministries of Education. Located in the campus of the University of the West Indies, the Institute has links with United States universities and nutritionists in each of the 17 member nations.

Managing iron deficiency anemia is a special interest of the Institute. CFNI helped to establish two nongovernmental organizations (NGOs) to aid in the Institute's work. One of these, based in Jamaica, prepares and distributes materials with financial support from UNICEF. The Caribbean Association of Nutritionists and Dietitians (CAND) develop text books, food composition tables and diet manuals. CFNI is developing stronger links with the French and Dutch speaking islands.

Ms. Catherine Siandwazi reported on the activities of the Commonwealth Regional Health Community Secretariat for East, Central and Southern Africa. The Secretariat serves the East, Central and Southern Africa (ECSA) Food and Nutrition Cooperation founded in 1979 as a forum for discussing common problems through annual meetings. ECSA provides training in maternal and child nutrition, surveillance, planning management, food service and policy development. The University of Zimbabwe offers degree training in food science and nutrition. This year ECSA will sponsor a scientific symposium on micronutrients.

Ms. Siandwazi indicated that the group plans to encourage applied research and produce a newsletter in the future. They are creating data banks and a directory of experts in the area. Personnel from several of the ECSA countries have participated in the Program Against Micronutrient Malnutrition (PAMM) training course. While very beneficial for the few able to attend, PAMM training in the United States is not a cost effective way of training the numbers of people needed at the regional level.

The countries belonging to the old British Commonwealth provide the core funding for ECSA through the Ministry of Health in each country. Namibia is the first non-Commonwealth country to join ECSA. At the next Health Minister's Conference in November 1993 they will discuss holding a post-ICN meeting and the country plans of action.

Dr. Mathurin Nago stated that west Africa did not have the history of collaboration in scientific activities developed through the Commonwealth activities. In addition language is a greater barrier. OAU is planning to discuss strengthening the nutrition unit at the June summit meeting. Africa is likely to see an increase in malnutrition over the next 20-30 years and needs to make better use of the support for nutrition generated by the ICN.

During the discussion, Dr. Patterson reported on a successful modular training program developed in the Caribbean directed to work study student. Local industry has made significant use of the program to train their personnel.

V. INPF Mission and Future Activities

Dr. Gabr briefly described the history of INPF and it mission of bringing together young scientists from developing countries for policy development and planning. The past INPF meetings focussed on cross-cutting issues related to policy and planning. To be useful for developing countries the outcome must be applicable at the local level. He stated that issues of importance include new problems in nutrition for LDCs, human resources, role of NGOs and industry and generation of the necessary political will to tackle nutrition problems.

Advocacy is an important component of INPF's role. This advocacy can be accomplished through publications and communication with key policy leaders. Dr. Gabr reported that Mr. Seifman had suggested INPF work through existing newsletters to provide policy planning articles. Dr. Kahn urged the group to provide new ideas which could attract funding.

During the discussion the following points were raised. Developing countries must plan nutrition programs carefully because of their limited human and financial resources. The current focus on micronutrients carries with it a danger that other equally important nutrition issues will be overlooked. Planners must be careful not to lose sight of the whole picture. Assessing training needs and how to provide for these needs is critical. Is what is being taught in formal education and training programs what is really needed? Sustainability is a critical concern and requires coordination of micronutrient efforts.

VII. Discussion of Next Steps

The group decided to work informally to develop objectives for INPF that would help identify effective policy planning needs for micronutrient programs. Using these objectives, INPF could solicit support from multilateral and bilateral donors in addition to USAID.

VIII. Adjournment

The meeting adjourned at 1810. The steering committee members agreed to meet for dinner on Monday, 8 March to continue discussion of INPF objectives. At that time the group presented Dr. Kahn and Dr. Frances Davidson with a written description of proposed objectives and activities for INPF (attached).

Signed Suzanne J. Harris Date April 15, 1993
INPF Secretariat

Appendix 21

INPF MEETING 7 MARCH, 1993, MT. MERU HOTEL, ARUSHA

The INPF meeting convened in Arusha March 07, 1993 feels that the goal, objectives and activities of INPF should be maintained.

The objectives of INPF are:

- to bring Nutritionists from the developing world together to share experiences, and to develop strategies for initiating and sustaining interventions for the solution of issues of concern to the developing world,

- to develop plans and programs put forward by program planners of the developing world,

- to disseminate information among them,

- to develop an advocacy capability to address policy/decision makers within an intersectoral context, particularly following the recent (1992) International Conference on Nutrition in Rome.

These objectives were fulfilled in the past by successful INPF activities supported by USAID and other agencies.

In view of the global interest in micronutrients which is mainly technical and specific, it is suggested that INPF should be involved in the following ways:

1. policy and planning which will cut across activities in the management of several micronutrients, and involve program planners at the local level,

2. advocacy to emphasize the role of micronutrients within the general nutrition programs of the countries,

3. development of mechanisms for the coordination of various micronutrient interventions between each other, as well as with the overall nutrition program,

.../2

4. development of strategies for human resource preparation for micronutrient interventions within the nutrition training programs of the countries,

5. elaboration of strategies and guidelines to ensure sustainability of micronutrient interventions.

All these activities will be developed from case studies in the developing countries.

Appendix 22

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INTERNATIONAL NUTRITION PLANNERS FORUM

AD HOC WORKSHOP

EFFECTIVE NUTRITION COMMUNICATION FOR BEHAVIORAL CHANGE

Thursday, September 30
10:00 a.m. - 1:00 p.m.

Hyatt Regency Hotel
Grevilia Room 2
Adelaide, Australia

Welcome and Introductions	Dr. Mamdouh Gabr Chair, INPF
Perspective of the U.S. Agency for International Development	Dr. Frances Davidson USAID Office of Nutrition
Summary of Sixth INPF Workshop	Dr. Gabr
Nutrition Communication - the Asian Experience	Dr. Aree Valyasevi Mahidol University Thailand
Nutrition Communication - the African Experience	Mrs. Julia Tagwireyi Ministry of Health, Zimbabwe
Nutrition Communication - the Caribbean Experience	Dr. Wynante Patterson Caribbean Food and Nutrition Center Jamaica
General Discussion	

235

Appendix 23

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SIXTH INPF
CONFERENCE REPORT
NOW AVAILABLE IN
SPANISH AND FRENCH

For Immediate Release
Contact: Dr. Suzanne Harris
(202) 659-9024

Washington, D.C.--As community-based nutrition interventions become more and more prevalent, learning the mechanisms of effective communication in promoting behavior change has become a critical step in planning successful programs. No longer the sole domain of professional nutritionists, nutrition interventions now require the collaboration of communications specialists, policy makers, and the health-care community. *Effective Nutrition Communication for Behavior Change* provides the key principles necessary for successful planning of collaborative interventions. The International Nutrition Planners Forum (INPF) is pleased to announce the release of this report in Spanish and French.

This report summarizes the Sixth International Conference of the INPF held 4-6 September 1991 in Paris, France. Participants from 18 developing countries were organized into country teams comprising a technical nutrition specialist, a nutrition practitioner responsible for nutrition education programs, and a media specialist. Each country team presented a case study of a nutrition communication program from their country. The report provides a synthesis of the discussions generated at the conference and the content of the case studies. The conference provided a unique hands-on learning experience, offering participants the opportunity to incorporate what they learned from the presentations into plans for new communication projects for their countries.

Also available from the INPF Secretariat is *Crucial Elements of Successful Community Nutrition Programs*, the report of the Fifth International INPF Conference, held in 1989 in Seoul, Korea. This report is also available in Spanish and French. Copies of both reports may be ordered from the INPF Secretariat, The Nutrition Foundation, Inc., 1126 Sixteenth Street, NW, Suite 700, Washington, DC, USA.

INPF is an informal organization of technical experts and professionals from developing countries with expertise and responsibility for nutrition and related policy and programs. It was established in 1981 through the initiative of the U.S. Agency for International Development to provide better opportunities and channels of discussion among developing country nutrition professionals.

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Appendix 24

The Nutrition Foundation
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JOINT MICRONUTRIENT CONSULTATIVE GROUP
MINUTES OF WORKING GROUP MEETING

14-15 JANUARY 1993
THE NUTRITION FOUNDATION
WASHINGTON, DC

I. Introduction

Dr. Abraham Horwitz called the meeting to order at 11:16 a.m. An attendance list and tentative agenda are attached. Dr. Horwitz opened the discussion by congratulating Richard Seifman and USAID for undertaking an effort to test the feasibility of coordinating micronutrient activities at the country-level. Mr. Seifman acknowledged that USAID supports testing of the hypothesis that a coordinated approach is feasible. He pointed to the emphasis placed on micronutrient malnutrition in the Declaration and Plan of Action from the International Conference on Nutrition (ICN). Countries will be developing national plans of action that will include strategies for controlling micronutrient deficiencies. Mr. Seifman referred to the Joint Micronutrient Mission as a methodology for others to improve upon. Countries will be looking for ways to formulate options for controlling micronutrient malnutrition.

The mission members agreed that written support from the Filipino government for the mission objectives and schedule was essential. The mission concept was raised with the Philippine Secretary of Health, Mr. Flavia, during the Program Against Micronutrient Malnutrition's (PAMM) Advocacy Week in Atlanta during December 1992. Mr. Seifman also discussed the concept with Dr. Tan, Philippine Undersecretary of Health, during the ICN meeting in Rome and with Mrs. Bayani, Philippine Department of Agriculture. In both instances the Philippine response was an enthusiastic willingness to cooperate.

The USAID mission is also supportive and pleased with the more sequential approach now being adopted. There are strong ties between the USAID mission and the Secretary of the Health, Mr. Flavia. The Secretary has the utmost confidence in Dr. Tan with whom the mission will communicate.

Dr. Horwitz pointed out the importance of the Filipino's understanding the Joint Micronutrient Mission benefits for them. Dr. West added that the mission team must also understand the Filipino expectations and work to make these compatible. They must be kept fully informed of the mission goals and be made aware that new funds from USAID for the Philippines is not a likely outcome. The ICN Plan of Action states that governments should adopt appropriate strategies to control micronutrient malnutrition and this mission will help the Filipino government identify feasible strategies. Partnership with the Filipinos

should be stressed, as well as the potential for developing a practical effective process for others to use.

Mr. Seifman asked that "ownership" of the mission be transferred to the Joint Micronutrient Mission team and that the secretariat will send a facsimile to Dr. Tan at the close of the day's session requesting an assurance of the Department's support for the mission. The secretariat will also share the revised scope of work with the Department and ask for their approval.

II. Work Session

A. Review of the proposed scope of work - The group generally agreed with the purposes for the mission, but questioned if these purposes were operational. It was agreed that the mission would review currently available data and determine the extent of overlap. The purpose of the mission is to evaluate a joint approach rather than individual micronutrient programs or options. Dr. Keith West agreed to draft an introductory paragraph linking the goals adopted at ICN to the mission purpose.

This paragraph along with other agreed upon changes will be incorporated into the scope of work by the secretariat and distributed to the mission team for review. After the mission team's further revisions are incorporated, the revised scope of work will be sent to Dr. Tan for Filipino input.

Exchange of technical information - The mission team discussed a wide range of contacts within the Philippines and data sources that should be pulled together before the team visits the Philippines. Individual contacts included: Rolf Klemm (country director for Helen Keller International); Department of Health contact - Dr. Roehas (worked on micronutrient section of ICN Plan of Action during Geneva PrepCom) and Dr. Reodica, Dr. Florentino Solon, Nutrition Center of the Philippines; Mr. Lim, Philippine Chamber of Food Manufacturers, Inc. (active at ICN micronutrient workshop); Dr. Rudolfo Florentino, Food and Nutrition Research Institute (planning a dietary intake survey for April '93); other donor agencies, FAO, WHO - Ian Darnton Hill, UNICEF, World Bank - Rae Gallaway; USAID mission in Manila; and others such as PAMM and ICCIDD.

Additional sources of data include: the ICN country paper from the Philippines, USAID library files; information about Nutri-Net (a computerized system being established in the Philippines); information about Filipino food laws and

regulations (Mr. V. Mannar - ICCIDD/UNICEF would be a good contact); Procter and Gamble (marketing vitamin A fortified "Star" margarine). The secretariat will ask Dr. Tan to identify specific Filipino expert counterparts - one for each of the three micronutrient.

The team members exchanged information about the most effective assessment and intervention strategies that might be applicable in the Philippines. Dr. John Dunn indicated that the most recent iodine deficiency prevalence data were collected in 1987. There are areas with high goiter prevalence generally in areas with limited accessibility. Urinary iodine is the best assessment methodology. Possible vehicles for iodine fortification include salt (80% of Philippine salt is sea salt), oil, and water. Procter and Gamble has approached ICCIDD asking for help in fortifying Star margarine which is already fortified with vitamin A. Cod liver oil is naturally high in iodine as well as vitamin A. Fish paste is another vehicle for multiple fortification. It contains iodine and possibly vitamin A and could be fortified with FeEDTA. Weaning foods are a likely vehicle, too.

Dr. Sam Kahn pointed out that Drs. Nevin Scrimshaw and Fernando Viteri are testing weekly vs. daily iron supplementation in pregnant women. Another possibility is a slow release tablet developed in Jamaica. In Indonesia gelatinized ferrous sulfate was tested successfully. Dr. Kavishe's group in Tanzania is evaluating iron supplementation compliance using computerized bottle caps. Dr. Dutra de Oliveira is testing iron fortification of water. Double fortification of rice with iron and vitamin A is being evaluated by Dr. Florentino.

Dr. West asked for information about fortification of supplement foods provided by the World Food Program and those provided for disaster relief.

The target age group was discussed. Prolonged breastfeeding can produce iron problems. Target age groups for iron and vitamin A is 3-5 years of age, but for iodine school age is preferable.

Dr. Jim Cook noted that the Philippines have a law requiring iron fortified rice but the rice millers are resisting fortification because of unfavorable taxation policy.

B. <u>Strategy for mission visit</u> - The group discussed the pros and cons of team members going their separate ways to gather

information during the visit, then discussing their findings as a group. Field trips to get an idea of "reality" were suggested. The group decided to utilize both individual activities to evaluate current prevalence data and combined team meetings with policymakers and industry.

A draft report outline should be developed before the team leaves for the Philippines. No cost estimates will be included. A second team meeting should be scheduled before the visit, hopefully at a time when Dr. Tan can participate.

Once again the team reiterated the meaning of the term "joint", i.e., both between the team and the Philippines and among the three micronutrient. The focus will be on developing options in areas of assessment, interventions and education that may include programs beyond micronutrient, e.g., expanded immunization program. The team will also assess the effectiveness of the process through which they developed these options. The visit should include individual meetings, field trips, and meetings with governmental representatives, with multinational organizations and with private sector interests. The group endorsed the idea of holding a meeting of all interested parties after the first week to generate discussion among the sectors on the feasibility of coordinated strategies. Overlap between micronutrients in target populations, food fortification vehicle or other components may be utilized, but the team will look for other coordination opportunities as well.

Mission logistics - The four team members - Dr. Horwitz, Dr. Dunn, Dr. Cook and Dr. West tentatively agreed to travel to the Philippines on June 12 (which is a Filipino holiday) and return on June 26, pending agreement with the USAID mission and the Department of Health. The secretariat will attempt to supply on the ground logistical support before and during the mission visit. Rolf Klemm, HKI, and Lenona De Angus, PATH, were suggested as possible persons for this task. The team members requested business class airline tickets and permission to work through weekends with per diem.

The Nutrition Foundation will serve as the secretariat for the mission collecting all available pertinent information and developing the draft report. These data will be summarized in a table format.

Dr. West agreed to develop a set of prevalence maps for the three micronutrient. Dr. Kahn agreed to develop evaluation criteria for judging the effectiveness of the process. He will

also maintain contact with the USAID mission and inform them of the mission expectations.

c. Timetable

January	Secretariat will revise scope of work and circulate to mission team, along with Philippine response when received.
February	Team members and secretariat will collect additional micronutrient information on the Philippines. Secretariat will schedule a second meeting or conference call in April based on Dr. Tan's schedule.
March	Secretariat will draft summary table and report outline for review by team. Dr. West's maps will be circulated as well.
April	Second meeting of team or conference call. Secretariat will make all necessary logistical arrangements.
May	
June	Mission to visit the Phillipines
July	Secretariat to complete mission report.

III Adjournment

Dr. Horwitz adjourned the meeting at 3:00 p.m. on 15 January reminding the group that the most worthwhile efforts are likely to occur before the visit. He viewed the mission as an important exercise but not a simple one.

NOTE: Dr. Tan and the Department of Health both responded very positively on 27 January (attached) to the secretariat's 14 January letter (also attached).

Signed: Suzanne S. Harris

Suzanne S. Harris

Date: March 4, 1993

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Joint Micronutrient Consultative Group
Minutes of Mission Planning Meeting

21 April 1993
The Nutrition Foundation, Inc.
Washington, D.C.

I. Welcome and Introduction

As chair for this discussion, Dr. Abraham Horwitz opened the meeting at 1915. Mr. Richard Seifman reported the excitement expressed by those learning of the mission to the Philippines and the hope that this mission will be a prototype for the Philippines and for other developing nations. The following meeting participants introduced themselves: Ms. Laurie Lindsay Aomari, Dr. Frances R. Davidson, Dr. Suzanne S. Harris, Dr. Jean Humphrey, Dr. Samuel G. Kahn, Dr. Jaime Z. Galvez Tan, and Dr. Keith P. West, Jr. (The agenda and participant list for this meeting are attached.)

II. General Discussion of Mission Objectives

Dr. Horwitz reviewed the mission's purpose and underscored the two-way process anticipated between Filipino professionals and the mission team. He emphasized that the Joint Micronutrient Consultative Group (JMCG) is considering what is common and what is feasible among assessments and interventions for vitamin A, iron, and iodine deficiencies. The JMCG mission team will do this for the purpose of the mission itself, for the benefit of the Philippines, and for the benefit of other countries.

Dr. Tan described several recent activities related to micronutrients in the Philippines. These have occurred as a result of the "23 in 93" exciting programs, projects, and activities described by Dr. Juan M. Flavier, Secretary of Health. Prevention of micronutrient malnutrition is number 21 of the "excitements." Related activities are

1. During the first 100 days of the new presidential administration, health workers exceeded their goal and distributed 242,000 iodine capsules to women in a mountainous region known to have endemic goiter. Plans are underway to include vitamin A distribution with the next round of iodine distribution.

2. Department of Health (DOH) staff met with the nation's largest salt manufacturer to discuss fortification of salt with iodine.

3. In May 1993, nine million children aged 12 months through five years will receive vitamin A supplements with immunizations during the second day of the annual immunization days. Mobilization of 300,000 volunteers for immunization days makes this an excellent opportunity to increase awareness of vitamin A deficiency.

4. The National Nutrition Council created the National Committee on Micronutrient Malnutrition (NCMM) chaired by Dr. Tan. This committee will examine program integration for vitamin A, iron, and iodine and includes governmental and nongovernmental organization representatives.

5. Within the National Nutrition Council, scientific teams of biochemists and clinicians were designated for each micronutrient and their first meeting is planned for the week of 19 April. These teams will operate over the next ten to 15 years.

6. Within the DOH, a multidisciplinary team called the Core Team on Micronutrient Malnutrition was identified. The team includes representatives of departments dealing with communications, laboratories, research, and epidemiology.

7. At the first NCMM meeting, a subcommittee on integrating the three micronutrient programs was established. Dr. Carmencita Reodica, Assistant Secretary, Office for Special Concerns, DOH, will chair the subcommittee. The group's first meeting was scheduled for 27 April.

Dr. Tan announced that due to a substantial increase in the DOH budget, sufficient funds are available to purchase adequate vitamin A, iodine, and iron supplements for distribution in the Philippines in 1993 and 1994. Other positive developments include a commitment from Kiwanis International to assist with the elimination of iodine deficiency, and provision of training by the Program Against Micronutrient Malnutrition for laboratory support, fortification, and communications. The World Bank Municipality Project in the Philippines also may have micronutrient components. Communications concerning DOH activities have contributed to bringing health into focus as a national concern in the Philippines. Dr. Tan stated that his country is planning to reach the micronutrient goals by 1995. The DOH looks forward to this partnership between the Philippines and the JMCG to strengthen and refine their work.

III. Discussion of Specific Activities to be a Part of the Philippine Visit

Dr. Tan outlined the tentative mission agenda:

14 June	Courtesy calls to USAID, DOH, National Nutrition Council
15 June	Briefing with National Committee on Micronutrient Malnutrition
16 June	Meetings with scientific expert groups for each micronutrient
17 June}	Field visit options: Visit a site where all three deficiencies occur
18 June}	or visit three different sites; land travel for each no more
19 June}	than five hours
20 June	No meetings scheduled
21 June}	
22 June}	Report preparation
23 June}	
24 June	Meeting with National Committee on Micronutrient Malnutrition
25 June	Exit conference with DOH (secretary, undersecretary, other staff)

Dr. Horwitz suggested meetings with food industry representatives and visits to laboratory facilities be added to the agenda. Dr. West said the visits should contribute to assessing where there is overlap in micronutrient activities and also where it is not sensible to encourage an overlap.

Dr. Tan disclosed that the visits will offer an opportunity to view micronutrient activities within the process of decentralization of health services. Beginning 1 April, 55% of the DOH budget will be reallocated to the provinces as part of decentralization. Some aspects of health services wiil be retained by the DOH, e.g., procurement of supplements. Immunizations will remain temporarily under the DOH but a strategic plan being prepared for infectious diseases may change that policy.

Dr. Davidson pointed out that visiting during decentralization may provide information about how to maintain enthusiasm for micronutrient malnutrition issues at various levels of government. Dr. West expressed concern that provincial food laws regarding fortification might develop in a decentralized system. This could potentially result in multiple sets of disparate regulations. Dr. Horwitz recommended increased attention to surveillance and monitoring to be sure that micronutrient malnutrition goals are still being achieved within a decentralized system. Two groups, Management Sciences for Health and the Field Epidemiology Training Program of CDC, are assisting DOH with work that will contribute to successful surveillance and monitoring activities.

On related issues, Dr. Tan stated that although rice fortification is legislated, operational problems continue; he commented that current rice subsidies help the entire population rather than a targeted group in need. Fortification of monosodium glutamate was tried unsuccessfully in the Philippines but fortification of margarine with vitamin A is now being considered. Sugar was mentioned as a potential vehicle for fortification. Dr. Tan observed that although fish sauce is used extensively, local and household production limit its potential as a suitable vehicle. There is increasing consumption of instant noodles made in the Philippines from imported wheat and these noodles are available at an affordable price. This product may be a suitable vehicle for fortification.

Dr. West inquired about commodity food distribution in the Philippines. Dr. Tan reported that CARE distributes bulgur wheat and peas through all schools and day care centers and that DOH provides some food assistance to children less than three years of age and pregnant women. Although these programs are extensive, there have been criticisms regarding the acceptability of the commodities provided. The system and the commodities may be changed. CARE's food delivery system has been successfully used to distribute family planning packages. Dr. West commented that this distribution program may provide possibilities for micronutrient interventions.

Dr. Tan noted the success of a UNICEF supported, Department of Agriculture program for biointensive gardening at the home, school, and village levels. Currently half of Philippine provinces have gardens at home and at school. Ninety percent of the produce is consumed in the home; ten percent is sold.

Other organizations contributing to micronutrient activities in the Philippines were mentioned by Dr. Tan. The Asian Development Bank is assisting with materials for local officials. IMPACT, a local nongovernmental organization, assisted with the recent successful distribution of iodine supplements and will assist with the planned vitamin A distribution in the same communities.

Dr. Kahn questioned whether the team should meet with donors during the mission. Dr. Tan requested that there be some coordination among donors--perhaps even before the mission--to guarantee that efforts undertaken in the Philippines are complementary. Dr. Horwitz recommended that this will be handled best if the Philippine government manages this coordination as far as possible.

Related events occurring in the Philippines close to the time of the JMCG mission include the Advocacy for Micronutrients Meeting (8-10 June) and National Nutrition Month (July). Mr. David Haxton will be in the Philippines for the advocacy meeting. The Core Team on Micronutrient Malnutrition is working with him to organize this meeting which will include the private sector.

IV. Discussion of Logistical Questions

Dr. Horwitz asked for identification of five individuals to work cooperatively with the JMCG mission team: a technical and operational counterpart, a counterpart for each nutrient, and a nongovernmental organization representative. Dr. Tan reported that counterparts for each micronutrient have been selected: Dr. Florentino Solon for vitamin A, Dr. Rodolfo Florentino for iron, and Dr. Virgilio Gonzales for iodine.

Dr. Horwitz asked if the Philippine government could arrange for necessary facilities and transportation within the Philippines for the mission team.

V. Adjournment

On behalf of the JMCG and the mission team, Dr. Horwitz expressed gratitude to Dr. Tan for the preparations underway by the DOH. Dr. Horwitz then closed the meeting at 2110.

Signed: Laurie Lindsay Aomari

Laurie Lindsay Aomari, RD

Date: 14 May 1993

attachments

JOINT MICRONUTRIENT CONSULTATIVE GROUP

Joint Micronutrient Mission Planning Meeting

21 April 1993
6:30 PM

The Nutrition Foundation, Inc.
1126 Sixteenth Street, N.W.
Washington, D.C.

TENTATIVE AGENDA

I. Welcome and Introductions

II. General Discussion of Mission Objectives

III. Discussion of Specific Activities to be a Part of the Philippine Visit

IV. Discussion of Logistical Questions

V. Adjournment

Joint Micronutrient Consultative Group (JMCG)

Joint Micronutrient Mission Planning Meeting
Washington, DC
21 April 1993

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Appendix 25

JOINT MICRONUTRIENT CONSULTATIVE GROUPS
Micronutrient Joint Mission

Terms of Reference

I. Introduction

Vitamin A, iodine and iron deficiencies represent a form of "Hidden Hunger" that can erode general health and resistance to infection, cause blindness, mental retardation and other more subtle developmental handicaps, and increase risk of mortality, particularly among young children. Pregnant women and the elderly may also be highly vulnerable to these deficiencies. The economic consequences of micronutrient deficiency to any nation are likely to be substantial.

In recent years the global community has affirmed its commitment to prevent vitamin A, iodine and iron deficiencies as public health problems by the year 2000, as avowed at the Summit for the World's Children and the "Ending Hidden Hunger" Conference in Montreal. In 1992 this commitment was strengthened by governments of the world in the form of a detailed Plan of Action at the International Conference on Nutrition (ICN) in Rome. Significantly, representatives of the Filipino Government helped to revise the language of the Plan on "Preventing Specific Micronutrient Deficiencies" at the Preparatory Committee meeting in Geneva in August 1992. This revision became the basic text for the Plan that was unanimously adopted in Rome in December 1992.

The ICN Plan of Action calls on governments, private enterprises, national organizations and international agencies to work together to assess micronutrient deficiencies, and to formulate and implement locally appropriate, effective, and sustainable preventive programs so that the year 2000 goals may be achieved. The Terms of Reference, proposed herein, represent a step toward meeting this challenge. It provides an opportunity for the Government, the private sector, and other sectors of the Philippines to join with an international team of experts in examining the extent of micronutrient deficiencies in the country and to explore ways to effect a coordinated, multiple micronutrient deficiency control strategy.

II. Purpose

1. Assess existing information on the extent and severity of vitamin A, iodine, and iron deficiencies, especially the degrees to which they may geographically and demographically overlap.

2. Describe past and current, public and private sector programs for assessing, monitoring, controlling and preventing each micronutrient deficiency.

3. Identify potential ways to coordinate a micronutrient deficiency assessment, control and prevention strategy that may improve efficiency, coverage and sustainability.

4. Prepare a report based on the "best judgement" of the joint mission participants which contains recommendations and proposes options to better address micronutrient malnutrition in the Philippines and other countries.

5. Evaluate the joint mission approach and its generality to other countries.

III. Scope of Work

A detailed scope of work will be developed to fulfill the "Purposes" described above. A preliminary draft is contained in Attachment A, but this will be reviewed and revised in consultation with appropriate Filipino representatives. Philippine inclusion in joint mission efforts is encouraged, the extent of such participation to be determined by the Government of the Philippines.

JOINT MICRONUTRIENT CONSULTATIVE GROUPS
Micronutrient Joint Mission

Scope of Work

A. Prior to Country Site Visit

Review pertinent published and unpublished reports on:

- prevalence and epidemiology of vitamin A, iodine and iron deficiencies in focus country;
- cross-sectional and surveillance-based approaches that have been in use to assess micronutrient malnutrition;
- interventions that have, to-date, been attempted to control and/or prevent each micronutrient deficiency, alone or combined and reported outcomes; and
- recent practical, innovative approaches (i.e. operationally feasible research).

Identify governmental and non-governmental counterparts who can provide additional, often local, reports on the micronutrient deficiencies.

Coordinate with USAID Office of Nutrition staff (alerting and informing USAID/Manila will be coordinated through the Office of Nutrition).

Plan for country visit, including:

- identify gaps in knowledge about the three micronutrient deficiencies;
- develop a preliminary list of individuals, institutions, government agencies, NGOs, donor agencies, industrial and commercial companies to visit;
- identify possible surveillance or survey sites, distribution programs, and commercial processes to see;
- prepare a list of questions to address country policies governing imports, tariffs, taxes, food and drug regulations and other pertinent laws that may directly affect future interventions; and
- through meetings, faxing, conference calling or other means by which the joint mission members can exchange information, discuss mission strategy and refine this scope of work.

B. During Country Visit

Meet with USAID/Manila staff.

Meet with the Secretary of Health and the Secretary of Agriculture as well as other Filipino government officials.

Meet with local counterparts to:

- clarify the two-week agenda;
- refine the meeting and site-visit schedule;
- review and update the team's current state of knowledge on micronutrient status and deficiency control/prevention in the country;
- discuss local views on current program strategies, coverage, efficiency and effectiveness; and
- identify areas for further investigation (based on gaps) dealing with prevalence, target groups, types of programs (supplementation, fortification, diet diversification, primary health care, etc.).

Meet with government, NGO, industry (e.g. sugar, salt, and other food and pharmaceutical companies), and bi- and multilateral donor agency representatives to discuss potential collaborative (and coordinated) solutions.

Meet with research and policy institutions to discuss a micronutrient focus to nutrition research agendas and national policy.

Site visit areas where more than one micronutrient deficiency is likely to exist.

Assess the availability of equipment for micronutrient production, qualtiy control, packaging and distribution; also what laboratory equipment is available for assessment, monitoring, treating and preventing deficiencies.

C. After Country Visit

Based on information collected prior to and during the country visit, prepare a report that recommends options in which multiple micronutrients can be combined or a coordination among individual systems could converge to mitigate micronutrient deficiencies. Include in the report a description of the micronutrient problem, major gaps in our knowledge base, and strategies which may offer opportunities to effect combined or coordinated control with rationale.

Specifically:

- identify each intervention system by micronutrient(s) and target

population(s);

- describe the feasibility and practical advantages of each system;
- identify micronutrient compounds to be used, dosage form and level;
- describe the systems to be used for monitoring the recommended interventions;
- describe when and how best to evaluate micronutrient programs; and
- identify potential strengths and constraints of each proposed option and discuss the sustainability of each.

The report also should identify which micronutrient systems (including management, distribution, evaluation) may best be carried out independently of the others and why.

In addition, the joint mission should evaluate the "short-term joint mission approach" as a mechanism for wider application.

The Nutrition Foundation
1126 SIXTEENTH STREET, N.W. • WASHINGTON, D.C. 20036 • (202) 659-9024

October 29, 1993

Agency for International Development
Office of Financial Management
Program Accounting and Finance Division
515 22nd Street, N.W. 7th Floor
Washington, DC 20006

Dear Sir or Madame:

Enclosed are the original and two copies of the Federal Cash Transactions Report (SF 272) and the Financial Status Report (SF 269) for Cooperative Agreement No. DAN-5115-A-00-7114-00 for the period July 1, 1993 through September 30, 1993.

If you have any questions concerning these reports, please do not hesitate to call me at (202) 659-9024.

Sincerely,

Suzanne S. Harris, Ph.D.
Project Director

Enclosures

cc: Ms. Brenda Colwell

262

FEDERAL CASH TRANSACTIONS REPORT

(See instructions on the back. If report is for more than one grant or assistance agreement, attach completed Standard Form 272-A.)

Approved by Office of Management and Budget, No. 80-R0182

1. Federal sponsoring agency and organizational element to which this rep is submitted: Agency for International Development, M/FM/PAFD

2. RECIPIENT ORGANIZATION

Name : The Nutrition Foundation, Inc.

Number and Street : 1126 16th Street, NW #700

City, State and ZIP Code: Washington, DC 20036

3. FEDERAL EMPLOYER IDENTIFICATION NO. ▶ 13-1624140

4. Federal grant or other identification number: 72008701

5. Recipient's account number identifying number: 13-1624140

6. Letter of credit number: 72001568

7. Last payment voucher number: 38

Give total number for this period

8. Payment Vouchers credited to your account: 2

9. Treasury checks received (*whether or not deposited*): 0

10. PERIOD COVERED BY THIS REPORT

FROM (*month, day, year*): 7/1/93

TO (*month, day year*): 9/30/93

11. STATUS OF FEDERAL CASH *(See specific instructions on the back)*

a. Cash on hand beginning of reporting period	$ 14,239.97
b. Letter of credit withdrawals	200,000.00
c. Treasury check payments	
d. Total receipts (*Sum of lines b and c*)	200,000.00
e. Total cash available (*Sum of lines a and d*)	214,239.97
f. Gross disbursements	109,269.57
g. Federal share of program income	485.50
h. Net disbursements (*Line f minus line g*)	108,784.07
i. Adjustments of prior periods	
j. Cash on hand end of period	$ 105,455.90

12. THE AMOUNT SHOWN ON LINE 11J, ABOVE, REPRESENTS CASH REQUIREMENTS FOR THE ENSUING _____ *Days*

13. OTHER INFORMATION

a. Interest income	$ 471.43
b. Advances to subgrantees or subcontractors	$

14. REMARKS (*Attach additional sheets of plain paper, if more space is required*)

15. CERTIFICATION

I certify to the best of my knowledge and belief that this report is true in all respects and that all disbursements have been made for the purpose and conditions of the grant or agreement

AUTHORIZED CERTIFYING OFFICIAL

SIGNATURE: Suzanne S. Harris

DATE REPORT SUBMITTED: 10/29/93

TYPED OR PRINTED NAME AND TITLE: Suzanne S. Harris, PhD
Project Director

TELEPHONE (*Area Code, Number, Extension*): 202-659-9024

THIS SPACE FOR AGENCY USE

FINANCIAL STATUS REPORT

(Follow instructions on the back)

1. FEDERAL AGENCY AND ORGANIZATIONAL ELEMENT TO WHICH REPORT IS SUBMITTED	Agency for International Development M/FM/PAFD
2. FEDERAL GRANT OR OTHER IDENTIFYING NUMBER	DAN-5115-A-00-7114-00
OMB Approved No. 80-R0180	0412-0510
PAGE OF	1 of 1 PAGES
3. RECIPIENT ORGANIZATION (Name and complete address, including ZIP code)	The Nutrition Foundation, Inc. 1126 16th Street, NW #700 Washington, DC 20036
4. EMPLOYER IDENTIFICATION NUMBER	13-1624140
5. RECIPIENT ACCOUNT NUMBER OR IDENTIFYING NUMBER	DAN-5115-A-00-7114-00
6. FINAL REPORT	☐ YES ☒ NO
7. BASIS	☐ CASH ☒ ACCRUAL
8. PROJECT/GRANT PERIOD (See instructions) FROM (Month, day, year)	10/1/87
TO (Month, day, year)	11/30/93
9. PERIOD COVERED BY THIS REPORT FROM (Month, day, year)	7/1/93
TO (Month, day, year)	9/30/93

10. STATUS OF FUNDS

PROGRAMS/FUNCTIONS/ACTIVITIES ►	(a) Vitamin A	(b) Anemia	(c) SUSTAIN	(d) INPF	(e) INNE	(f)	TOTAL (g)
a. Net outlays previously reported	$2,572,186.91	$ 872,329.21	$ 898,508.72	$ 443,124.54	$ 96,583.31	$	$4,882,732.69
b. Total outlays this report period	72,078.88	30,811.09	.00	6,379.60	.00		109,269.57
c. *Less:* Program income credits	485.50	.00	.00	.00	.00		485.50
d. Net outlays this report period *(Line b minus line c)*	71,593.38	30,811.09	.00	6,379.60	.00		108,784.07
e. Net outlays to date *(Line a plus line d)*	2,643,780.29	903,140.30	898,508.72	449,504.14	96,583.31		4,991,516.76
f. *Less:* Non-Federal share of outlays	935,243.80	361,661.27	405,096.76	71,928.93	18,041.90		1,791,972.66
g. Total Federal share of outlays *(Line e minus line f)*	1,708,536.49	541,479.03	493,411.96	377,575.21	78,541.41		3,199,544.10
h. Total unliquidated obligations							
i. *Less:* Non-Federal share of unliquidated obligations shown on line h							
j. Federal share of unliquidated obligations							
k. Total Federal share of outlays and unliquidated obligations	1,708,536.49	541,479.03	493,411.96	377,575.21	78,541.41		3,199,544.10
l. Total cumulative amount of Federal funds authorized	1,849,355.00	638,731.00	493,412.00	417,477.00	77,289.00		3,476,264.00
m. Unobligated balance of Federal funds	140,818.51	97,251.97	.04	39,901.79	(1,252.41)		276,719.90

11. INDIRECT EXPENSE

a. TYPE OF RATE *(Place "X" in appropriate box)* ☒ PROVISIONAL ☐ PREDETERMINED ☐ FINAL ☐ FIXED

b. RATE	c. BASE	d. TOTAL AMOUNT	e. FEDERAL SHARE
12%	97,562.11	11,707.46	11,707.46

12. REMARKS: *Attach any explanations deemed necessary or information required by Federal sponsoring agency in compliance with governing legislation.*

13. CERTIFICATION

I certify to the best of my knowledge and belief that this report is correct and complete and that all outlays and unliquidated obligations are for the purposes set forth in the award documents.

SIGNATURE OF AUTHORIZED CERTIFYING OFFICIAL: Suzanne S. Harris

DATE REPORT SUBMITTED: 10/29/93

TYPED OR PRINTED NAME AND TITLE: Suzanne S. Harris, PhD Project Director

TELEPHONE (Area code, number and extension): 202-659-9024

269 102

STANDARD FORM 269 (7-76)
Prescribed by Office of Management and Budget
Cir. No. A-110

FINANCIAL SUMMARY FOR THE FOURTH QUARTER, 1993
JULY 1, 1993 THROUGH SEPTEMBER 30, 1993

	VITAMIN A	ANEMIA	SUSTAIN	INPF	INNE	TOTAL
DIRECT LABOR	12,776.49	8,883.23	0.00	1,044.81	0.00	22,704.53
FRINGE BENEFITS	3,275.95	2,176.25	0.00	267.87	0.00	5,720.07
TEMPORARY HELP	0.00	0.00	0.00	0.00	0.00	0.00
CONSULTANTS	3,900.00	2,400.00	0.00	0.00	0.00	6,300.00
PUBLICATIONS & SUPPORT	27,108.51	4,336.35	0.00	2,092.97	0.00	33,537.83
TRAVEL	2,091.17	2,062.64	0.00	199.90	0.00	4,353.71
PER DIEM	2,661.39	2,661.41	0.00	1,114.10	0.00	6,436.90
SUPPLIES	567.41	198.90	0.00	61.49	0.00	827.80
EQUIPMENT PURCHASE	0.00	0.00	0.00	0.00	0.00	0.00
OFFICE LEASE	2,496.34	1,386.20	0.00	119.74	0.00	4,002.28
GENERAL EXPENSES	476.38	236.55	0.00	10.85	0.00	723.78
FISCAL ADMINISTRATION	1,053.15	582.49	0.00	50.73	0.00	1,686.37
COMMUNICATIONS	7,949.35	2,585.88	0.00	733.61	0.00	11,268.84
MEETING ROOM RENTAL	0.00	0.00	0.00	0.00	0.00	0.00
TOTAL DIRECT	64,356.14	27,509.90	0.00	5,696.07	0.00	97,562.11
INDIRECT (12%)	7,722.74	3,301.19	0.00	683.53	0.00	11,707.46
TOTAL AMOUNT	72,078.88	30,811.09	0.00	6,379.60	0.00	109,269.57
NET OUTLAYS PREVIOUSLY REPORTED (a)	2,572,186.91	872,329.21	898,508.72	443,124.54	96,583.31	4,882,732.69
TOTAL OUTLAYS THIS REPORT PERIOD (b)	72,078.88	30,811.09	0.00	6,379.60	0.00	109,269.57
LESS: PROGRAM INCOME CREDITS (c)	485.50	0.00	0.00	0.00	0.00	485.50
NET OUTLAYS THIS REPORT PERIOD (d)	71,593.38	30,811.09	0.00	6,379.60	0.00	108,784.07
NET OUTLAYS TO DATE (e)	2,643,780.29	903,140.30	898,508.72	449,504.14	96,583.31	4,991,516.76
LESS: NON-FEDERAL SHARE OF OUTLAY (f)	935,243.80	361,661.27	405,096.76	71,928.93	18,041.90	1,791,972.66
TOTAL FEDERAL SHARE OF OUTLAYS (g)	1,708,536.49	541,479.03	493,411.96	377,575.21	78,541.41	3,199,544.10
TOTAL UNLIQUIDATED OBLIGATIONS (h)	0.00	0.00	0.00	0.00	0.00	0.00
TOTAL CUM. FED. FUNDS AUTHORIZED (i)	1,849,355.00	638,731.00	493,412.00	417,477.00	77,289.00	3,476,264.00
UNOBLIGATED BALANCE OF FED. FUNDS (m)	140,818.51	97,251.97	0.04	39,901.79	(1,252.41)	276,719.90
IN KIND (this period)	0.00	0.00	0.00	0.00	0.00	0.00
IN KIND (cumulative)	862,408.61	86,607.95	397,555.00	67,652.00	14,908.00	1,429,131.56
NON REIMBURSABLE (this period)	0.00	0.00	0.00	0.00	0.00	0.00
NON REIMBURSABLE (cumulative)	72,835.19	275,053.32	7,541.76	4,276.93	3,133.90	362,841.10

PROJECTED EXPENDITURES Q1 FY94 (EXTENSION PERIOD)
OCTOBER 1, 1993 THROUGH NOVEMBER 30, 1993

	VITAMIN A	ANEMIA	SUSTAIN	INPF	INNE	TOTAL
DIRECT LABOR	10,000.00	4,500.00	0.00	1,000.00	0.00	15,500.00
FRINGE BENEFITS	3,300.00	1,485.00	0.00	330.00	0.00	5,115.00
TEMPORARY HELP	250.00	0.00	0.00	0.00	0.00	250.00
CONSULTANTS	0.00	0.00	0.00	0.00	0.00	0.00
PUBLICATIONS & SUPPORT	4,250.00	1,050.00	0.00	0.00	0.00	5,300.00
TRANSLATION	0.00	0.00	0.00	0.00	0.00	0.00
TRAVEL	4,000.00	3,600.00	0.00	0.00	0.00	7,600.00
PER DIEM	1,000.00	1,500.00	0.00	0.00	0.00	2,500.00
SUPPLIES	1,100.00	900.00	0.00	200.00	0.00	2,200.00
EQUIPMENT PURCHASE	0.00	0.00	0.00	0.00	0.00	0.00
OFFICE LEASE	2,300.00	1,350.00	0.00	200.00	0.00	3,850.00
GENERAL EXPENSES	600.00	400.00	0.00	100.00	0.00	1,100.00
FISCAL ADMINISTRATION	200.00	100.00	0.00	50.00	0.00	350.00
COMMUNICATIONS	2,000.00	800.00	0.00	400.00	0.00	3,200.00
MEETING ROOM RENTAL	0.00	0.00	0.00	0.00	0.00	0.00
TOTAL DIRECT	29,000.00	15,685.00	0.00	2,280.00	0.00	46,965.00
INDIRECT (12%)	3,480.00	1,882.20	0.00	273.60	0.00	5,635.80
TOTAL AMOUNT	32,480.00	17,567.20	0.00	2,553.60	0.00	52,600.80

The Nutrition Foundation
1126 SIXTEENTH STREET, N.W. • WASHINGTON, D.C. 20036 • (202) 659-9024

October 29, 1993

Agency for International Development
Office of Financial Management
Program Accounting and Finance Division
515 22nd Street, N.W. 7th Floor
Washington, DC 20006

Dear Sir or Madame:

Enclosed are the original and two copies of the Federal Cash Transactions Report (SF 272) and the Financial Status Report (SF 269) for Cooperative Agreement No. DAN-5115-A-00-7114-00 for the period July 1, 1993 through September 30, 1993.

If you have any questions concerning these reports, please do not hesitate to call me at (202) 659-9024.

Sincerely,

Suzanne S. Harris, Ph.D.
Project Director

Enclosures

cc: Ms. Brenda Colwell

261

FINANCIAL STATUS REPORT

(Follow instructions on the back)

1. FEDERAL AGENCY AND ORGANIZATIONAL ELEMENT TO WHICH REPORT IS SUBMITTED: Agency for International Development M/FM/PAFD	2. FEDERAL GRANT OR OTHER IDENTIFYING NUMBER: DAN-5115-A-00-7114-00	OMB Approved No. 80-R0180 0412-0510	PAGE 1 OF 1 PAGES	
3. RECIPIENT ORGANIZATION (Name and complete address, including ZIP code): The Nutrition Foundation, Inc. 1126 16th Street, NW #700 Washington, DC 20036	4. EMPLOYER IDENTIFICATION NUMBER: 13-1624140	5. RECIPIENT ACCOUNT NUMBER OR IDENTIFYING NUMBER: DAN-5115-A-00-7114-00	6. FINAL REPORT ☐ YES ☒ NO	7. BASIS ☐ CASH ☒ ACCRUAL
	8. PROJECT/GRANT PERIOD (See instructions) FROM (Month, day, year): 10/1/87 TO (Month, day, year): 11/30/93		9. PERIOD COVERED BY THIS REPORT FROM (Month, day, year): 7/1/93 TO (Month, day, year): 9/30/93	

10. STATUS OF FUNDS

PROGRAMS/FUNCTIONS/ACTIVITIES ►	(a) Vitamin A	(b) Anemia	(c) SUSTAIN	(d) INPF	(e) INNE	(f)	TOTAL (g)
a. Net outlays previously reported	$2,572,186.91	$ 872,329.21	$ 898,508.72	$ 443,124.54	$ 96,583.31	$	$4,882,732.69
b. Total outlays this report period	72,078.88	30,811.09	.00	6,379.60	.00		109,269.57
c. *Less:* Program income credits	485.50	.00	.00	.00	.00		485.50
d. Net outlays this report period (*Line b minus line c*)	71,593.38	30,811.09	.00	6,379.60	.00		108,784.07
e. Net outlays to date (*Line a plus line d*)	2,643,780.29	903,140.30	898,508.72	449,504.14	96,583.31		4,991,516.76
f. *Less:* Non-Federal share of outlays	935,243.80	361,661.27	405,096.76	71,928.93	18,041.90		1,791,972.66
g. Total Federal share of outlays (*Line e minus line f*)	1,708,536.49	541,479.03	493,411.96	377,575.21	78,541.41		3,199,544.10
h. Total unliquidated obligations							
i. *Less:* Non-Federal share of unliquidated obligations shown on line h							
j. Federal share of unliquidated obligations							
k. Total Federal share of outlays and unliquidated obligations	1,708,536.49	541,479.03	493,411.96	377,575.21	78,541.41		3,199,544.10
l. Total cumulative amount of Federal funds authorized	1,849,355.00	638,731.00	493,412.00	417,477.00	77,289.00		3,476,264.00
m. Unobligated balance of Federal funds	140,818.51	97,251.97	.04	39,901.79	(1,252.41)		276,719.90

11. INDIRECT EXPENSE

a. TYPE OF RATE (*Place "X" in appropriate box*) ☒ PROVISIONAL ☐ PREDETERMINED ☐ FINAL ☐ FIXED

b. RATE	c. BASE	d. TOTAL AMOUNT	e. FEDERAL SHARE
12%	97,562.11	11,707.46	11,707.46

12. REMARKS: *Attach any explanations deemed necessary or information required by Federal sponsoring agency in compliance with governing legislation.*

13. CERTIFICATION

I certify to the best of my knowledge and belief that this report is correct and complete and that all outlays and unliquidated obligations are for the purposes set forth in the award documents.

SIGNATURE OF AUTHORIZED CERTIFYING OFFICIAL: Suzanne S. Harris

DATE REPORT SUBMITTED: 10/29/93

TYPED OR PRINTED NAME AND TITLE: Suzanne S. Harris, PhD Project Director

TELEPHONE (*Area code, number and extension*): 202-659-9024

269-102

STANDARD FORM 269 (7-76)
Prescribed by Office of Management and Budget
Cir. No. A-110

FEDERAL CASH TRANSACTIONS REPORT

(See instructions on the back. If report is for more than one grant or assistance agreement, attach completed Standard Form 272-A.)

Approved by Office of Management and Budget, No. 80-R0182

1. Federal sponsoring agency and organizational element to which this report is submitted: Agency for International Development, M/FM/PAFD

2. RECIPIENT ORGANIZATION

Name : The Nutrition Foundation, Inc.

Number and Street : 1126 16th Street, NW #700

City, State and ZIP Code: Washington, DC 20036

3. FEDERAL EMPLOYER IDENTIFICATION NO. ▶ 13-1624140

4. Federal grant or other identification number: 72008701

5. Recipient's account number or identifying number: 13-1624140

6. Letter of credit number: 72001568

7. Last payment voucher number: 38

Give total number for this period

8. Payment Vouchers credited to your account: 2

9. Treasury checks received (whether or not deposited): 0

10. PERIOD COVERED BY THIS REPORT

FROM (*month, day, year*): 7/1/93

TO (*month, day year*): 9/30/93

11. STATUS OF FEDERAL CASH *(See specific instructions on the back)*

a. Cash on hand beginning of reporting period	$ 14,239.97
b. Letter of credit withdrawals	200,000.00
c. Treasury check payments	
d. Total receipts (*Sum of lines b and c*)	200,000.00
e. Total cash available (*Sum of lines a and d*)	214,239.97
f. Gross disbursements	109,269.57
g. Federal share of program income	485.50
h. Net disbursements (*Line f minus line g*)	108,784.07
i. Adjustments of prior periods	
j. Cash on hand end of period	$ 105,455.90

12. THE AMOUNT SHOWN ON LINE 11J, ABOVE, REPRESENTS CASH REQUIREMENTS FOR THE ENSUING _____ *Days*

13. OTHER INFORMATION

a. Interest income	$ 471.43
b. Advances to subgrantees or subcontractors	$

14. REMARKS (*Attach additional sheets of plain paper, if more space is required*)

15. CERTIFICATION

I certify to the best of my knowledge and belief that this report is true in all respects and that all disbursements have been made for the purpose and conditions of the grant or agreement

AUTHORIZED CERTIFYING OFFICIAL

SIGNATURE: Suzanne S. Harris

DATE REPORT SUBMITTED: 10/29/93

TYPED OR PRINTED NAME AND TITLE: Suzanne S. Harris, PhD
Project Director

TELEPHONE (*Area Code, Number, Extension*): 202-659-9024

THIS SPACE FOR AGENCY USE

FINANCIAL SUMMARY FOR THE FOURTH QUARTER, 1993
JULY 1, 1993 THROUGH SEPTEMBER 30, 1993

	VITAMIN A	ANEMIA	SUSTAIN	INPF	INNE	TOTAL
DIRECT LABOR	12,776.49	8,883.23	0.00	1,044.81	0.00	22,704.53
FRINGE BENEFITS	3,275.95	2,176.25	0.00	267.87	0.00	5,720.07
TEMPORARY HELP	0.00	0.00	0.00	0.00	0.00	0.00
CONSULTANTS	3,900.00	2,400.00	0.00	0.00	0.00	6,300.00
PUBLICATIONS & SUPPORT	27,108.51	4,336.35	0.00	2,092.97	0.00	33,537.83
TRAVEL	2,091.17	2,062.64	0.00	199.90	0.00	4,353.71
PER DIEM	2,661.39	2,661.41	0.00	1,114.10	0.00	6,436.90
SUPPLIES	567.41	198.90	0.00	61.49	0.00	827.80
EQUIPMENT PURCHASE	0.00	0.00	0.00	0.00	0.00	0.00
OFFICE LEASE	2,496.34	1,386.20	0.00	119.74	0.00	4,002.28
GENERAL EXPENSES	476.38	236.55	0.00	10.85	0.00	723.78
FISCAL ADMINISTRATION	1,053.15	582.49	0.00	50.73	0.00	1,686.37
COMMUNICATIONS	7,949.35	2,585.88	0.00	733.61	0.00	11,268.84
MEETING ROOM RENTAL	0.00	0.00	0.00	0.00	0.00	0.00
TOTAL DIRECT	64,356.14	27,509.90	0.00	5,696.07	0.00	97,562.11
INDIRECT (12%)	7,722.74	3,301.19	0.00	683.53	0.00	11,707.46
TOTAL AMOUNT	72,078.88	30,811.09	0.00	6,379.60	0.00	109,269.57
NET OUTLAYS PREVIOUSLY REPORTED (a)	2,572,186.91	872,329.21	898,508.72	443,124.54	96,583.31	4,882,732.69
TOTAL OUTLAYS THIS REPORT PERIOD (b)	72,078.88	30,811.09	0.00	6,379.60	0.00	109,269.57
LESS: PROGRAM INCOME CREDITS (c)	485.50	0.00	0.00	0.00	0.00	485.50
NET OUTLAYS THIS REPORT PERIOD (d)	71,593.38	30,811.09	0.00	6,379.60	0.00	108,784.07
NET OUTLAYS TO DATE (e)	2,643,780.29	903,140.30	898,508.72	449,504.14	96,583.31	4,991,516.76
LESS: NON-FEDERAL SHARE OF OUTLAY (f)	935,243.80	361,661.27	405,096.76	71,928.93	18,041.90	1,791,972.66
TOTAL FEDERAL SHARE OF OUTLAYS (g)	1,708,536.49	541,479.03	493,411.96	377,575.21	78,541.41	3,199,544.10
TOTAL UNLIQUIDATED OBLIGATIONS (h)	0.00	0.00	0.00	0.00	0.00	0.00
TOTAL CUM. FED. FUNDS AUTHORIZED (i)	1,849,355.00	638,731.00	493,412.00	417,477.00	77,289.00	3,476,264.00
UNOBLIGATED BALANCE OF FED. FUNDS (m)	140,818.51	97,251.97	0.04	39,901.79	(1,252.41)	276,719.90
IN KIND (this period)	0.00	0.00	0.00	0.00	0.00	0.00
IN KIND (cumulative)	862,408.61	86,607.95	397,555.00	67,652.00	14,908.00	1,429,131.56
NON REIMBURSABLE (this period)	0.00	0.00	0.00	0.00	0.00	0.00
NON REIMBURSABLE (cumulative)	72,835.19	275,053.32	7,541.76	4,276.93	3,133.90	362,841.10

PROJECTED EXPENDITURES Q1 FY94 (EXTENSION PERIOD)
OCTOBER 1, 1993 THROUGH NOVEMBER 30, 1993

	VITAMIN A	ANEMIA	SUSTAIN	INPF	INNE	TOTAL
DIRECT LABOR	10,000.00	4,500.00	0.00	1,000.00	0.00	15,500.00
FRINGE BENEFITS	3,300.00	1,485.00	0.00	330.00	0.00	5,115.00
TEMPORARY HELP	250.00	0.00	0.00	0.00	0.00	250.00
CONSULTANTS	0.00	0.00	0.00	0.00	0.00	0.00
PUBLICATIONS & SUPPORT	4,250.00	1,050.00	0.00	0.00	0.00	5,300.00
TRANSLATION	0.00	0.00	0.00	0.00	0.00	0.00
TRAVEL	4,000.00	3,600.00	0.00	0.00	0.00	7,600.00
PER DIEM	1,000.00	1,500.00	0.00	0.00	0.00	2,500.00
SUPPLIES	1,100.00	900.00	0.00	200.00	0.00	2,200.00
EQUIPMENT PURCHASE	0.00	0.00	0.00	0.00	0.00	0.00
OFFICE LEASE	2,300.00	1,350.00	0.00	200.00	0.00	3,850.00
GENERAL EXPENSES	600.00	400.00	0.00	100.00	0.00	1,100.00
FISCAL ADMINISTRATION	200.00	100.00	0.00	50.00	0.00	350.00
COMMUNICATIONS	2,000.00	800.00	0.00	400.00	0.00	3,200.00
MEETING ROOM RENTAL	0.00	0.00	0.00	0.00	0.00	0.00
TOTAL DIRECT	29,000.00	15,685.00	0.00	2,280.00	0.00	46,965.00
INDIRECT (12%)	3,480.00	1,882.20	0.00	273.60	0.00	5,635.80
TOTAL AMOUNT	32,480.00	17,567.20	0.00	2,553.60	0.00	52,600.80

The Nutrition Foundation
1126 SIXTEENTH STREET, N.W. • WASHINGTON, D.C. 20036 • (202) 659-9024

29 October 1993

Ms. Brenda J. Colwell
Project Officer
Office of Nutrition
Bureau for Research and Development
Agency for International Development
SA-18, Room 411
Washington, DC 20523-1808

Dear Ms. Colwell:

Enclosed are five (5) copies of the report on the activities of The Nutrition Foundation, Inc. related to Cooperative Agreement No. DAN-5115-A-00-7114-00 during the fourth quarter of fiscal year 1993.

If you have any questions, please do not hesitate to contact me at (202) 659-9024.

Sincerely,

Suzanne S. Harris, Ph.D.
Project Director

Enclosures

cc: Mr. Michael B. Gushue
Dr. Alex Malaspina
Ms. Sharon Coleman
AID, POL/CDIE/DI

Quarterly Report

Cooperative Agreement No. DAN-5115-A-00-7114-00

Fourth Quarter, FY93

1 July - 30 September 1993

GENERAL MANAGEMENT AND ADMINISTRATION

Reports

The Q3FY93 report and Financial Statement were submitted to the AID project officer on 29 July 1993.

Administration

Mrs. Molly Hovermale left her temporary position as Administrative Assistant on 28 September 1993. The position remained vacant at the end of the quarter. The Nutrition Foundation will advertise for a replacement during Q1FY94.

INDIVIDUAL PROGRAM ACTIVITIES

International Vitamin A Consultative Group (IVACG)

1. XVI IVACG Meeting

During this quarter the secretariat provided IVACG information, general meeting information, and suggestions regarding the formation of a local committee for the meeting to Dr. Kraisid Tontisirin and other colleagues at the Institute of Nutrition at Mahidol University (INMU). These colleagues suggested changing the meeting site to Chiang Rai, Thailand, to take advantage of better facilities and transportation while offering convenience for meeting participants from Myanmar, China, and other countries in the region. The IVACG Steering Committee was advised of this change and consulted about the possible meeting dates suggested by Thai colleagues, i.e., 24-28 October 1994 and 14-18 November 1994. Based on responses from steering committee members and preferences of Thai colleagues, 24-28 October was chosen as the time for

the meeting. Steering committee members had no objections to holding the meeting in Chiang Rai.

The secretariat provided a draft letter for the USAID Mission in Thailand to Dr. Davidson.

A memo to the IVACG Steering Committee from the secretariat requested views regarding the meeting theme. The following options were suggested as potential themes: 1. Vitamin A as part of national plans of action for nutrition, 2. Sustainability of vitamin A programs, and 3. Dietary interventions for vitamin A deficiency. Feedback will be instrumental in developing the call for abstracts. The call for abstracts will be circulated to more than 800 individuals and institutions during the next quarter. Meeting plans will be discussed during the IVACG Steering Committee meeting in Q1FY94.

Ms. Aomari communicated with INMU colleagues about plans for a site visit in November 1993. This visit will include discussions with members of the local committee for the meeting and with individuals from organizations that may wish to provide additional support to the local committee, negotiations regarding meeting facilities and hotel rooms, and investigation of banking possibilities. Ms. Aomari will also assess customs, shipping, transportation, and other details necessary to ensure a successfully organized meeting. At the close of the quarter, tentative arrangements for this were in progress in coordination with INMU colleagues. Approval for this international travel was requested from the Office of Nutrition.

2. XV IVACG Meeting

During this quarter *Toward Comprehensive Programs to Reduce Vitamin A Deficiency: A Report of the XV International Vitamin A Consultative Group Meeting* was completed. Of the 1400 copies printed, more than 800 copies have been distributed. Response to the meeting report has been very positive. Multiple copies of this publication were distributed to the Office of Nutrition, IVACG Steering Committee members, IVACG regional representatives for Africa, meeting rapporteurs, local committee leaders, and financial contributors. UNICEF and FAO requested larger shipments for distribution among agency staff worldwide. Single copies were provided to all meeting participants. A letter of thanks accompanied the copies mailed to presenters, session chairs, and rapporteurs. Modest honorariums were provided for the meeting rapporteurs.

A draft letter was prepared for use by Mr. Richard Seifman in distribution of the report. Dr. Davidson distributed copies of the meeting report at the XV International Congress of Nutrition in Adelaide.

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International Nutritional Anemia Consultative Group (INACG)

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Eight hundred copies of the iron EDTA monograph, *Iron EDTA for Food Fortification*, were printed. Copies were distributed to the authors, reviewers, EDTA manufacturers, and food companies that produce iron fortified products. A news release was prepared and distributed to the mailing list maintained by the Nutrition Foundation. The secretariat hand delivered copies of the monograph to Dr. Graeme Clugston and Dr. Ken Bailey in the Nutrition Division of WHO and to Dr. John Herrman of the Joint FAO/WHO Expert Committee on Food Additives. Copies were also hand delivered to Mr. John Lupien at FAO.

Dr. Frances Davidson, Office of Nutrition, USAID, announced the availability of the monograph at the XV International Congress of Nutrition in Adelaide, Australia. The secretariat arranged for copies of the monograph and order forms to be available at the Congress.

The secretariat continued discussions with Mr. Francisco Mardones, World Bank, and Dr. Dick Uiterwaal, a consultant for the World Bank, regarding an iron fortification project they are planning in Ecuador. The secretariat put them in contact with Dr. John Vanderveen and Dr. Paul Whittaker at the U.S. Food and Drug Administration to get additional safety information. Dr. Sean Lynch reviewed the calculations performed by Dr. Uiterwaal to determine the concentration of iron EDTA necessary in the supplemental foods being prepared for the Ecuador project.

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The secretariat reviewed a draft Executive Summary of the mission report and provided comments to Ms. Lynnda Keiss.

International Nutrition Planners Forum (INPF)

1. Report of the Sixth INPF Conference "Effective Nutrition Communication for Behavioral Change"

Eight hundred copies of the French translation of Sixth INPF Conference summary were printed. A news release describing the availability of this translation and the Spanish translation was sent to the Nutrition Foundation mailing list.

2. INPF Steering Committee

The secretariat arranged for the steering committee members already attending the XV International Congress of Nutrition in Adelaide, Australia, to hold an informal meeting. The secretariat also arranged for a meeting room in which the steering committee held an ad hoc workshop to discuss the findings of the Sixth INPF Conference and prepared a tentative agenda based on Dr. Gabr's direction. This workshop was held on Thursday, 30 September 1993 with Dr. M. Gabr as the chair. Dr. Frances Davidson, USAID, participated in the workshop. The secretariat arranged for copies of the report of the Sixth INPF Conference, *Effective Communication for Behavioral Change*, in English, French, and Spanish and order forms to be available in the workshop room.

3. Information Requests

The secretariat responded to 86 requests for *Effective Nutrition Communication for Behavioral Change* and *Crucial Elements of Successful Community Nutrition Programs* in Q3FY93.

Quarterly Report

Cooperative Agreement No. DAN-5115-A-00-7114-00

Fourth Quarter, FY93

1 July - 30 September 1993

GENERAL MANAGEMENT AND ADMINISTRATION

Reports

The Q3FY93 report and Financial Statement were submitted to the AID project officer on 29 July 1993.

Administration

Mrs. Molly Hovermale left her temporary position as Administrative Assistant on 28 September 1993. The position remained vacant at the end of the quarter. The Nutrition Foundation will advertise for a replacement during Q1FY94.

INDIVIDUAL PROGRAM ACTIVITIES

International Vitamin A Consultative Group (IVACG)

1. XVI IVACG Meeting

During this quarter the secretariat provided IVACG information, general meeting information, and suggestions regarding the formation of a local committee for the meeting to Dr. Kraisid Tontisirin and other colleagues at the Institute of Nutrition at Mahidol University (INMU). These colleagues suggested changing the meeting site to Chiang Rai, Thailand, to take advantage of better facilities and transportation while offering convenience for meeting participants from Myanmar, China, and other countries in the region. The IVACG Steering Committee was advised of this change and consulted about the possible meeting dates suggested by Thai colleagues, i.e., 24-28 October 1994 and 14-18 November 1994. Based on responses from steering committee members and preferences of Thai colleagues, 24-28 October was chosen as the time for

the meeting. Steering committee members had no objections to holding the meeting in Chiang Rai.

The secretariat provided a draft letter for the USAID Mission in Thailand to Dr. Davidson.

A memo to the IVACG Steering Committee from the secretariat requested views regarding the meeting theme. The following options were suggested as potential themes: 1. Vitamin A as part of national plans of action for nutrition, 2. Sustainability of vitamin A programs, and 3. Dietary interventions for vitamin A deficiency. Feedback will be instrumental in developing the call for abstracts. The call for abstracts will be circulated to more than 800 individuals and institutions during the next quarter. Meeting plans will be discussed during the IVACG Steering Committee meeting in Q1FY94.

Ms. Aomari communicated with INMU colleagues about plans for a site visit in November 1993. This visit will include discussions with members of the local committee for the meeting and with individuals from organizations that may wish to provide additional support to the local committee, negotiations regarding meeting facilities and hotel rooms, and investigation of banking possibilities. Ms. Aomari will also assess customs, shipping, transportation, and other details necessary to ensure a successfully organized meeting. At the close of the quarter, tentative arrangements for this were in progress in coordination with INMU colleagues. Approval for this international travel was requested from the Office of Nutrition.

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The International Life Sciences Institute's (ILSI) Human Nutrition Institute, of which the Nutrition Foundation is a division, has initiated jointly with FAO the development of a food-based strategies manual for controlling micronutrient malnutrition. An organizational meeting was held in Rome on 20-22 September 1993.

ILSI submitted comments to the U.S. Department of Agriculture and the U.S. Department of Health and Human Services on 7 September 1993 regarding the development of the U.S. Plan of Action in response to the International Conference on Nutrition. In these comments, ILSI urged continued support for USAID's efforts in controlling micronutrient malnutrition and urged strong support for food fortification, based on sound scientific criteria in the plan.

7. Joint Micronutrient Consultative Groups (JMCG)

The Secretariat paid all allowable expenses for the members of the Joint Micronutrient Mission Team for their trip to the Philippines. The secretariat

reimbursed the Philippine Department of Health for expenses incurred related to the teams's visit. The secretariat also drafted thank you letters for Dr. Horwitz, Chairman of the Mission Team, to send and sent a letter of appreciation to Mr. Rolf Klemm, Helen Keller International, for his help in organizing the mission.

The secretariat reviewed a draft Executive Summary of the mission report and provided comments to Ms. Lynnda Keiss.

International Nutrition Planners Forum (INPF)

1. Report of the Sixth INPF Conference "Effective Nutrition Communication for Behavioral Change"

   Eight hundred copies of the French translation of Sixth INPF Conference summary were printed. A news release describing the availability of this translation and the Spanish translation was sent to the Nutrition Foundation mailing list.

2. INPF Steering Committee

   The secretariat arranged for the steering committee members already attending the XV International Congress of Nutrition in Adelaide, Australia, to hold an informal meeting. The secretariat also arranged for a meeting room in which the steering committee held an ad hoc workshop to discuss the findings of the Sixth INPF Conference and prepared a tentative agenda based on Dr. Gabr's direction. This workshop was held on Thursday, 30 September 1993 with Dr. M. Gabr as the chair. Dr. Frances Davidson, USAID, participated in the workshop. The secretariat arranged for copies of the report of the Sixth INPF Conference, *Effective Communication for Behavioral Change*, in English, French, and Spanish and order forms to be available in the workshop room.

3. Information Requests

   The secretariat responded to 86 requests for *Effective Nutrition Communication for Behavioral Change* and *Crucial Elements of Successful Community Nutrition Programs* in Q3FY93.