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FUNCTIONAL SIGNIFICANCE OF MARGINAL NUTRIENT DEFICIENCIES: PROGRAM-PROJECT PLANNING

By

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Prepared For

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and the Joint Research Committee

Board for International Food and Agricultural Development

SECOND QUARTERLY REPORT ON THE FUNCTIONAL

SIGNIFICANCE OF MARGINAL NUTRIENT DEFICIENCIES

Workshops on Intake and Function

The arrangements have been completed for the five workshops on nutrient intake and function to be held in September, October and November, 1978. Table 1 contains a list of the dates and locations of the workshops.

TABLE 1
DATES AND LOCATIONS OF THE WORKSHOPS ON
NUTRIENT INTAKE AND FUNCTION

Disease Response:	September 25-29 Red Jacket Beach Motor Inn, Hyannis, Massachusetts
Cognitive and Sensory Ability:	October 2-6 Joseph Henry Building, National Academy of Sciences, Washington, D.C.
Reproductive Competency:	October 23-27 Torrey Pines Inn, La Jolla, California
Physical Activity and Work Output:	October 30-November 3 Torrey Pines Inn, La Jolla, California
Social Competency:	November 27-December 1 Westward Look Hotel, Tucson, Arizona

There have been some changes recently with regard to authors of the principal background papers. An updated and final list of authors is given in Table 2. Dr. Josef Brozek will prepare the paper for cognitive and sensory ability from the biological perspective while Dr. Henry Ricciuti will write from the social science viewpoint. Dr. John Bongaarts will write from the social science perspective for reproductive competency. Dr. C. Gopalan has agreed to prepare a piece on social

TABLE 2
AUTHORS OF PRINCIPAL BACKGROUND PAPERS (REVISED);
BIOLOGICAL AND SOCIAL SCIENCE PERSPECTIVES

Disease Response

Biological: R.K. Chandra, Memorial University of Newfoundland

Social: J.O. Field, Massachusetts Institute of Technology

Cognitive and Sensory Ability

Biological: J. Brozek, Lehigh University

Social: H. Ricciuti, Cornell University

Reproductive Competency

Biological: D. Picou, University of the West Indies

Social: J. Bongaarts, Population Council, New York City

Work Performance

Biological: F. Viteri, Institute of Nutrition of Central America and Panama

Social: C.J. Bliss, Nuffield College, Oxford, England

Social Competency

Biological: C. Gopalan, Indian Council of Medical Research, Hyderabad, India

Social: P. Ratoosh, Psychiatric Consultant, Berkeley, California

competency from the biological viewpoint although he will be unable to attend the workshop. At the time of this writing we have received the background papers from Drs. Chandra, Field, and Brozek and they have been included in Appendix 1.

Table 3 contains a revised list of participants in the workshops; however, there may be further changes and additions. Each workshop consists of sixteen to eighteen participants. In addition to experts in the workshop topic and in nutrition per se, we have included experts in anthropology, sociology, psychology, economics, epidemiology, and statistics, some of whom have done research on nutritional problems. Many people were invited to attend one of the workshops that could not participate, usually because of previous committments. Table 4 shows those people who were invited but were not able to attend.

The chairmen and rapporteurs for the workshops have been chosen as follows:

Workshop	Chairman	Rapporteur
Disease Response	G. Beaton	H. Sandstead
Cognitive Development	L. Greene	A. Harper
Reproductive Competency	A. Chavez	L. Graveti
Physical Activity and Work Output	M. Latham	R. Nesheim
Social Competency	M. Yarrow	P. Payne

TABLE 3
WORKSHOP PARTICIPANTS (REVISED)

Disease Response - September 25-29, Hyannis, Massachusetts

G. Beaton, University of Toronto

A. Block, University of California, Berkeley (observer)

D. Calloway, University of California, Berkeley

R.K. Chandra, Memorial University of Newfoundland

J.O. Field, Tufts University

G.S. Gershoff, Tufts University

L. Greene, University of Massachusetts

J.P. Habicht, Cornell University

J.L. Joy, University of California, Berkeley

G. Keusch, Mount Sinai Medical Center

T. Kramer, Washington University, St. Louis

E. Messer, Yale University

B. Morgan, Old Dominion University

H. Sandstead, Agriculture Research Service, U.S. Department of Agriculture

L. Schuman, University of Minnesota

G. Solimano, Columbia University

C. Wood, University of California, Berkeley

Cognitive and Sensory Development - October 2-6, Washington, D.C.

A. Block, University of California, Berkeley (observer)

J. Brozek, Lehigh University

D. Calloway, University of California, Berkeley

E. Foulks, University of Pennsylvania

Cognitive and Sensory Development - cont.

J. Galler, Massachusetts Institute of Technology

L. Greene, University of Massachusetts

A. Harper, University of Wisconsin

D.M. Hegsted, Human Nutrition Center, U.S. Department of Agriculture

H. Jacobs, U.S. Army Natick Laboratories

S. Margen, University of California, Berkeley

A. Meyer, United States Agency for International Development

M. Monk, New York Medical College

E. Pollitt, University of Texas

H. Ricciuti, Cornell University

W. Shoemaker, The Salk Institute

C. Wood, University of California, Berkeley

M. Yarrow, National Institutes of Health

Reproductive Competency - October 23-27, La Jolla, California

E. Barrett-Connor, University of California, San Diego

J. Bongaarts, Population Council, New York City

N. Butte, University of California, Berkeley (observer)

D. Calloway, University of California, Berkeley

A. Chavez, Instituto Nacional de la Nutricion, Mexico City

R. Frisch, Harvard University

J. Galler, Massachusetts Institute of Technology

L. Graveti, University of California, Davis

J. Joe, Navajo Community College, Tsaile, Arizona

R. Martorell, Stanford University

Reproductive Competency - cont.

D. Picou, University of the West Indies

P. Rosso, Columbia University

H. Srebnik, University of California, Berkeley

E. Thorbecke, Cornell University

B. Winikoff, Population Council, New York City

C. Wood, University of California, Berkeley

Work and Physical Activity - October 30-November 3, La Jolla, California

M. Barnett, Cornell University

S. Basta, World Bank

C. Bliss, Nuffield College, Oxford, England

R. Beall, University of California, Berkeley (observer)

K. Borer, University of Michigan

N. Borhani, University of California, Davis

E. Buskirk, Pennsylvania State University

D. Calloway, University of California, Berkeley

R. Evenson, Yale University

A. Ferro-Luzzi, University of California, Berkeley (visiting)

E. Fleischman, Advanced Research Resources Organization, Bethesda, Maryland

M. Latham, Cornell University

E. Montgomery, Washington University, St. Louis

R. Nesheim, Quaker Oats Company

S. Parker, Office of Population Censuses and Surveys, London, England

L. Schuman, University of Minnesota

F. Viteri, INCAP, Guatemala City

C. Wood, University of California, Berkeley

Social Competency - November 27-December 1, Tucson, Arizona

M. Behar, World Health Organization (tentative)

A. Berg, World Bank

D. Calloway, University of California, Berkeley

S. Chafkin, Ford Foundation

N. Cheek, Jr., Texas A&M University

C.W. Churchman, University of California, Berkeley

S. Greenhouse, George Washington University

G. Harrison, University of Arizona

J.L. Joy, University of California, Berkeley

R. Khare, University of Virginia

R. Livingston, University of California, San Diego Medical School

P. Payne, London School of Hygiene and Tropical Medicine

P. Ratoosh, Berkeley, California

V. Ruttan, University of Minnesota

W. Twining, University of Warwick

B. Winikoff, Population Council, New York City

C. Wood, University of California, Berkeley

TABLE 4
INVITED BUT UNABLE TO ATTEND

Disease Response

E.A. Alluisi, Performance Assessment Laboratory, Old Dominion University

T. Almy, Dartmouth Medical School

J. Austin, Harvard School of Public Health

M. Behar, Nutrition Division, World Health Organization

W. Beisel, U.S. Army Medical Research, Institute of Infectious Diseases

H. Fabrega, Department of Psychiatry, Pittsburgh, Pennsylvania

J. Galler, Massachusetts Institute of Technology

P. Greenwald, Cancer Control Bureau, New York State Department of Health

M. Grossman, Wadsworth Veterans' Hospital, University of California, Los Angeles

B. Kean, Cornell University

C. Lieber, Mt. Sinai School of Medicine

R. Olson, St. Louis University School of Medicine

H. Popper, Mt. Sinai School of Medicine

W. Sodeman, University of Tampa Medical College

S.G. Srikantia, National Institute of Nutrition, Indian Council of Medical Research, Hyderabad, India

L. Teply, United Nations Children's Fund

P. Timmer, Harvard University School of Public Health

Cognitive and Sensory Development

F. Bloom, Salk Institute

S. Dornbusch, Stanford University

H. Gelfand, University of Illinois

S. Greenhouse, George Washington University

Cognitive and Sensory Development - cont.

N. Howell, University of Toronto

J. Kagan, Harvard University

K.E. Knutsson, Swedish International Development Agency

B. Popkin, University of North Carolina

R. Shekelle, Rush Medical College

S. Snyder, Johns Hopkins University School of Medicine

R. Wurtman, Massachusetts Institute of Technology

Reproductive Competency

J. Blake, University of California, Los Angeles

R. Chez, Howard University

D. Glass

G. Harrison, University of Arizona

A. Hermalin, Ann Arbor, Michigan

R. Jaffee, University of California at San Francisco Medical Center

J. Knodel, Ann Arbor, Michigan

P.H. Leiderman, Stanford University

R. Pitkin, University of Iowa

R. Potter, Brown University

K.N. Raj, Center for Development Studies, Trivandrum, Kerala, India

Z. Stein, Columbia University (could not be reached)

M. Susser, Columbia University (could not be reached)

J.M. Tanner, Institute of Child Health

L. Teply, United Nations Children's Fund

E. Widdowson, Cambridge, United Kingdom

C. Yarbrough, Kenwood, California

Work and Physical Activity

P. Bardhan, University of California, Berkeley

C. Gotsch, Stanford University

D.M. Hegsted, Human Nutrition Center, U.S. Department of Agriculture

Social Competency

T. Almy, Dartmouth Medical School

G. Bateson, Ben Lomond, California

J. Cohen, Cornell University

S. Dornbusch, Stanford University

M. Douglass, Russell Sage Foundation

C. Gopalan, Indian Council of Medical Research, Hyderabad, India

J. Mayer, Tufts University

universities and colleges, and site visits to U.S. institutions.

A preliminary scoring sheet has been designed for use in evaluating the institutional returns. Each curriculum vitae submitted would be scored according to the following criteria:

Main discipline noted

Nutrient(s) with which investigator is primarily concerned

Training (score of 1-3; considering degree attained, school where degree obtained, field of degree)

Research (human or other)

Sub-disciplines noted

Publications in referreed journals:
- Number of publications dealing with human research
- For each program area (disease response, reproduction, etc.), the number of articles with a high degree of relevance, involving energy-protein malnutrition and the program area (score of 3); moderately relevant, only involving the program area (score of 2); slightly relevant (score of 1)
- Articles pertinent to food intake or nutrition indicators were also counted (relevance 1-3)
- Number of publications dealing with animal or biochemical research relevant to each program area scored similarly
- Relevant training/experience in each program area (score 0-3)
- Experience in less developed countries (score 0-3)
- Availability (for new research project) (score 0-3)

At this point, the publications of all of the curriculum vitae have been scored. The steering group will discuss these evaluations and perhaps modify the above criteria before further scoring is done. A decision will be made as to how total scores should be reached for each curriculum vitae and for each institution. There should be some way of absorbing key people in institutions which otherwise are not top-scorers. Possible consortia of institutions will be discussed. Criteria will be established for evaluation of each institution, its facilities, research

potential, and its links with overseas institutions. Site visits to possibly eligible U.S. institutions should be made at the beginning of 1979 and steering group members may make some of these visits. A second steering group meeting will be held after the workshops are all completed and the date for this meeting will be decided.

Site Visits

Three site visits have been made so far to institutions in less developed countries to appraise their potential for carrying out the sort of research that will ultimately be proposed in this program. Dr. D. Calloway visited the Indonesian Nutrition Research and Development Center in Bogor and attended the Workshop on Food and Nutrition in Indonesia held by the Indonesian Academy of Science. She also visited the Philippines. Dr. C. Wood made a preliminary site visit to the Bureau of Nutrition in Port-au-Prince, Haiti. The report of Dr. Calloway's visit to Indonesia is contained in Appendix 2. The other two reports will be included in the next quarterly report.

Nutrient Intake and Disease Response

R.K.Chandra

APPENDIX 1 PRINCIPAL BACKGROUND PAPERS

The availability and the provision of enough food for the continuously increasing population of the world is the greatest material problem facing mankind today. Associated with it is the stark spectrum of about 500 million people suffering from the multiple erosive effects of undernutrition; it is a rude eye opener for any serious student of global health situation.

NUTRITION, ENVIRONMENT, BIOLOGY AND GENES

The ability of an individual to achieve his/her optimal potential is dependent upon a harmonious interaction of genes, nutrition and environment. Nutritional stress affects each and every structure and function of the body. The effects of undernutrition are protean; some are adaptive changes with no apparent consequence, others are pathological and produce symptoms and signs; some are almost immediate and may be short-lived and reversible, others are prolonged or even permanent. All these effects are, however, conditioned and modulated by the genetic endowment (metabolic, immunologic, etc.) of the individual, by their timing in relation to the critical periods of growth and development of biological activities, and by the environment including socioeconomic and cultural factors. Thus there is an intimate interaction between genes, biological clocks, nutrition and environment; the effects of nutrient intake on disease response are also governed by such interactions.

The most prominent association of nutritional deficiency is with infection. However, these two inextricably intertwined problems defy easy analysis in terms of the underlying mechanisms of pathogenesis and interplay. Recent studies have revealed impaired function of a variety of host protective factors in malnourished individuals. It is possible that the clinical problem of repeated and severe infections in undernourished persons is the result of a summation of variable individual abnormalities in several key cellular and humoral immunological functions. These changes in immunocompetence may play a critical role in the effectiveness of immunization, in the susceptibility to septicemia spread of infection, and in the production of immunopathological disease. Infection itself can result in significant deficits in immunity function and in nutrition,

the latter because a sick individual has no desire to eat, intestinal absorption is impaired, and there are greater metabolic needs and heightened catabolic losses. In addition, there is sequesteration of many nutrients in an attempt to synthesize urgently needed antibodies, complement and other protective responses.

At the same time, it must be recognized that nutritional status is intricately tied to other health factors, and that the roots of malnutrition are largely economic and socio-cultural. To tackle this major world affliction, we must consider a portfolio approach of intervention at several levels, including socioeconomic development, nutrition education, promotion of breast feeding, immunizations, safe water supply, and environmental sanitation.

The task looks formidable, but that is no reason for not trying.

SUSCEPTIBILITY OF UNDERNOURISHED INDIVIDUALS TO INFECTION

The common association of malnutrition and infection does not necessarily imply a causal relationship. It must be recognized that the same economic, sociocultural and ecological factors which contribute to undernutrition may well maintain a high frequency of infectious diseases. In this connection, the role of poor personal hygiene and environmental sanitation, and early weaning with inadequate and inappropriate replacement needs to be highlighted.

A variety of evidences have been cited to support the cinical impression of health professionals working in developing countries that infections occur more frequently and are more severe in the malnourished. Epidemiologic data from field surveys in Asia and the Americas have confirmed the intimate association of nutritional deficiencies, growth failure, infectious illness and diarrhoeal disease. In a prospective study of Mexican children followed from birth to 5 years of age, moderate malnutrition correlated significantly with the duration and severity of infectious episodes and to a lesser extent with the incidence of diarrhoeal disease in the age period from 8 to 18 months. The majority of hospitalized children with severe forms of malnutrition have an associated infection at the time of admission; this is more often observed in kwashiorkor than in marasmus. The PAHO survey of mortality patterns in Central and South America showed that 57 percent of the children who died under 5 years of age revealed signs of nutritional growth retardation, intrauterine and/or postnatal, as either the primary or an associated cause of death, often from infection.

Many diseases run a more severe course in nutritionally deprived children. For example, measles is known to produce fatal giant cell pneumonia in kwashiorkor. Interestingly, there is an unexplained geographic difference in measles-associated morbidity and mortality; the firghtening spectrum of measles in African children with kwashiorkor has not been observed in Asian malnourished populations. Herpes virus infection is often generalized and fatal in kwashiorkor; autopsy studies show multiple visceral hemorrhages and there is a conspicuous lack of inflammatory response. Septicemia with Gram negative organisms and Pneumocytis carinii pneumonia frequently complicate moderate-severe protein-energy malnutrition. In undernourished populations, there is a heavier load of parasites, particularly Ascaris, Necator americanus,

Srongyloides stercoralis, Giardia lamblia and Entamoeba histolytica, and greater rates of infections with enteropathogens such as Shigella. Pneumonia and diarrhoea occur more frequently and are more severe, leading to higher death rate. Hepatitis B surface antigen is detected more often. The intimate association of tuberculosis and inanition so well described by Osler has been validated. However, tuberculosis and parasitic infestation may be the cause and/or the effect of undernutrition.

Whereas there is considerable data on energy-protein malnutrition, similar critical information for deficiency of specific nutrients is not available. This is understandable since malnutrition in man involves deficits of many elements, and each nutrient may exert a variable, possibly even opposing, influence on the occurrence of infection. Some surveys reported a decreased in infection rate among iron-supplemented infants, others have failed to detect such an association. Iron deficiency was noted to be a common denominator of chronic mucocutaneous candidiasis, and therapy with iron improved the skin lesions as well as the associated immunological changes. An association of increased infections and iron-deficiency anemia was seen in Indonesian plantation workers, although the study results were vitiated by unintentional provision of additional cash incentive, and by the lack of co current observations in a control group. Again, a Tanzanian study suggesting a lower infection rate in iron-defcient subjects than in those with other types of anemia had no control data on healthy subjects. In laboratory animals, deprivation of specific nutrients generally increases host susceptibility to pathogens and infection-related mortality.

IMMUNE RESPONSE IN NUTRITIONAL DEFICIENCY

In the last decade, many studies have looked at the ability of the undernourished subject to mount immune responses to specific antigenic challenge. Some have employed a uniform preplanned protocol (adapted from WHO-sponsored documents) and in a few instances, samples were analyzed or rechecked in a central reference laboratory.

The consistent demonstration of impaured cell-mediated immunity has been extensively reported. Several types of evidences were collected: Cutaneous delayed hypersensitivity to a battery of ubiquitous recall antigens or after deliberate immunization or sensitization, number of circulating thymus-dependent T lymphocytes, lymphocyte DNA synthesis induced by mitogens and antigens, production of soluble mediators of immune reactivity, mixed lymphocyte response and skin homografts.

Several methodological fallacies need to be pointed out for the correct interpretation and comparison of results. Skin responses require the participation of several cell types and their mediators, and depends upon nonimmunological dermal characteristics as well. Three separate components of such reactions are recognized; the afferent link of sensitization of T lymphocytes with or without prior processing by macrophages, the efferent link of antigen-recognition and proliferation of T lymphocytes and release of lymphokines, and finally the inflammatory response amplified by chemotactic factors. Impairment of one or more of these sequential steps will depress skin response. Lymphocyte stimulation in vitro depends upon the number and concentration of cells, other leukocytes and the amount of mitogen. It is ideal to plot a dose-response curve since the optimal concentration of mitogen required to produce maximal response may vary from one cell preparation to another, from one batch of mitogen to the other.

Most of the studies have shown a reduction in the number of circulating T cells, as detected by rosetting with sheep erythrocytes. It is possible that a change in the surface charge or in membrane-bound enzymes, eg cholinesterase, in malnutrition affects the detectable numbers of such cells. This change in T cell number is an early indicator of nutritional deficiency and is promptly reversed within 1-6 weeks on supplemental nutritional therapy. There is a relative increase in the number of 'null' cells; these cells suppress the functions of other lymphocytes and are cytotoxic for a variety of xenogeneic tissues in culture. Mitogen-induced lymphocyte DNA synthesis is reduced, except for one report from Chile on marasmic infants. Leukocyte migration inhibition factor is normal. Skin reponses are usually depressed.

Serum levels of immunoglobulins are generally elevated and IgG turnover is increased. In a rare infant with early onset malnutrition, serum IgG level may be low with a compensatory increased in plasma half-life. In most instances, antibody response to an adequate antigenic challenge is normal. Antigens requiring the help of T cells fare less well. Secretory IgA and mucosal antibody responses are significantly decreased; this may be the result of reduced number of IgA-producing plasma cells in jejunal and other submucosal locations, or reduced synthesis of secretory component, or both. Impaired mucosal immunity may facilitate the development of septicemia and of food antibodies. Data on antibody affinity is conspicuously lacking. In animals, however, protein deprivation results in a reduction in affinity of antibody, poorer and slower clearance of the antigen, and increased incidence of immune complexes.

Opsonic activity is related to the concentration of plasma employed in the in vitro techniques. When tested at concentration of 5% or higher, opsonization is comparable for sera of healthy and undernourished subjects. However, at greater dilutions, serum of malnourished children shows reduced capacity to opsonize particles for phagocytosis. Ingestion by neutrophils is normal but intracellular killing of pathogens is reduced. The importance of using a discriminatory ratio of bacteria to phagocytes has been reported.

Recently, we have looked at the number and location of intra-epithelial lymphocytes which are thymus-dependent and probably mediate cellular reactions in the mucosa. These cells are reduced in the epithelium of malnourished subjects. Experiments in animals suggest that such a change is the result largely of thymic involution associated with malnutrition. A 'leakage' of these cells into dilated lymphatics of the villus has been postulated.

Many other nonspecific protective factors are affected by nutritional deficiency, eg complement system, interferon, lysozyme, structural tissue changes, etc.

EFFECTS OF INFECTION ASSOCIATED WITH MALNUTRITION

Infection itself can produce significant changes in nutritional status and in immunity function. The extent of such alterations is determined by the severity and duration of illness, nature of the microbe, and the health status of the individual prior to infection. Febrile illnesses increase tissue catabolism and urinary losses, reduce appetite, decrease absorption or actually cause protein-losing enteropathy. In addition, the synthesis of acute phase reactant proteins, antibodies and other protective factors results in 'sequestration' of many nutrients, causing further nutritional deficiency. Infection depresses many aspects of immunity, possibly by alterations in hormonal balance, actual invasion of lymphoid tissues, endotoxemia, altered ratios of lymphocyte subpopulations, chalones, etc. Measles suppresses cellular immunity, may precipitate edema, and be followed by secondary infections including tuberculosis. These immunologic alterations have prognostic significance. Infection-induced granulocyte dysfunction may adversely influence the outcome of infectious illness.

IMMUNIZATION OF MALNOURISHED INDIVIDUALS

Since nutritional deficiency is associated with impaired immune responses, the effectiveness of vaccination must be carefully examined. The extensive literature on antibody responses to bacterial, viral and rickettsial antigens shows that in general, serum antibody response following adequate immunization is normal and that suboptimal response in undernourished subjects can be improved upon by giving a larger dose of the antigen, choosing appropriate adjuvants and excluding serious concomitant infection. In the reports of reduced conversion rate and antibody level following poliovirus administration, there was no correlation attempted with nutritional status. Virus "take" was generally associated with positive antibody response. The response improved and was comparable with titers achieved in industrialized countries when the vaccine was given 5 times. Some malnourished children show a secondary booster response following the apparently primary immunization, thereby suggesting previous exposure and memory even though antibody was not detectable prior to vaccination.

There is paucity of data on local mucosal antibody response in malnutrition. This has been examined only in one study, in which the presence and levels of secretory IgA-antibody to measles and poliovirus vaccines were significantly reduced.

There is limited information on cell-mediated immunity following immunization. After BCG vaccination, tuberculin conversion is observed to be less frequent in malnourished subjects. Similar data was obtained in small-for-gestation low birth weight infants.

The critical question in this area is the correlation between nutritional status and protective immunity to infection rechallenge irrespective of the magnitude of the immune response. Protective titres of antibody in man are not well defined for many infections. It is conceivable that the lower antibody levels in malnutrition may still be effective in warding off natural disease. Also, careful studies are required to look at the incidence, nature and severity of complications in immunized malnourished children following exposure to the pathogens in the natural community setting. Moreover, most studies of immunity-nutrition interactions have looked at severe forms of malnutrition, which constitute only 1-2% of the iceberg of nutritional deficiency. The responses and the immunity of individuals with mild-moderate deficiencies and of those with deficits of isolated nutrients, eg iron, vitamin A, should be evaluated. Based on current data, there is full justification for continuing mass scale comprehensive immunization programmes, perhaps with some additional reinforcing measures, and excluding only those with severe kwashiorkor.

INTERVENTIONS AFFECTING THE MALNUTRITION-INFECTION COMPLEX

While there is obvious need for obtaining more critical data on the etiopathogenetic interactions and biological significance of nutritional deficiencies and susceptibility to infectious disease, there should be attempts at tackling these twin problems by employing a variety of intervention strategies. These measures would in addition yield useful information on nutrient intake and the individual's response to stress and disease. Some of the immunologic approaches are briefly touched upon. Breast feeding is associated with reduced frequency of diarrhoea and respiratory infections, in both developing and industrialized countries. Complications such as dehydration and septicemia are prevented. Immunization schedules should be made more effective by modifying the dose of antigen, number of inoculations, timing in relation to nutritional status, type of adjuvant, and perhaps providing short-term nutritional supplements in selected instances. Immunopotentiation with biological or pharmacological agents may have some value, if it used as a short-term measure before an imminent stress, such as infection or surgery, in malnourished subjects. Short-term nutritional supplements before or during a period of metabolic stress, eg infection, may reduce the impairment of immunity associated with such episodes. This is particularly relevant for hospitalized patients. Specific nutrients may be required in individual subjects. Prevention of low birth weight by appropriate prepregnancy, antenatal and perinatal measures, will reduce the incidence of impaired immunocompetence associated with fetal growth retardation. Such defects of immunity occurring during intrauterine life are more severe and longer lasting, particularly in those who continue to have physical growth retardation. The strategies dealing with this problem must necessarily take into account the prevalence of various risk factors for causing low birth weight (preterm, or small-for-gestation, or both) and the magnitude of risk associated with each of these factors.

NUTRITIONAL STATUS OF HOSPITALIZED PATIENTS

In recent years, there has been increasing recognition of the frequent prevalence of energy-protein undernutrition in patients hospitalized for a variety of indications. This is true of children as well as adults. In such subjects, there is a good correlation between the presence of nutritional deficiencies, and infections and mortality. In patients with lymphomas and leukemias, the occurrence of complicating P.carinii infection was related to low concentrations of serum proteins and albumin, confirming controlled observations in protein-deficient animals. Nutritional deficiency in patients admitted to hospital for elective surgery has been shown to correlate with their ability to mount delayed hypersensitivity skin reactions to common recall antigens or chemical sensitizing agents. Postoperative sepsis and mortality correlated with preoperative serum albumin and transferrin levels, and with cutaneous anergy and lower phagocyte bactericidal capacity. Nutritional support may reverse these nutritional and immunologic changes and reduce the incidence of pyogenic infections and of death.

NUTRITION AND CANCER

The possible relationships between diet, nutrition, immunity and cancer are difficult to study and to interpret. One cannot generalize since no single etiopathogenetic factor underlies all cancers. If dietary factors do contribute to the development or progression of neoplasms, it is very likely that different types of malignant tumours are susceptible to dietary manipulations to a varying extent. Much of the data in this field is derived from observations in laboratory animals in whom the etiology of cancer can be defined.

In experimental animals, diet and tumour growth are intimately linked. It has been hypothesized that malignant cells divide and grow by deriving nutrients from the host whose nutritional status should affect tumorogenesis. Chronic calorie restriction reduced the incidence and delayed the appearance of many but not all tumours. This may be mediated by the inhibitory effect of energy deficiency on mitotic activity. In the case of mammary cancer in mice, caloric deprivation influences neoplastic proliferation possibly by reducing the production of estrogen, a cocarcinogen. Changes in the levels of glucocorticoids occur in malnourished subjects and may influence the genesis and growth of cancer tissue. On the other hand, obesity and tumour risk often run in parallel. Increased total amount of fat and a high proportion of polyunsaturated fats in the diet enhance susceptibility to cancer. Fat may act as a solvent for ingested carcinogens, thereby increasing the rate of carcinogen transfer. A diet high in polyunsaturated fatty acids promotes the synthesis of bile salts which provide the substrate for carcinogen-forming microorganisms implicated in the etiology of colonic cancer. Others have failed to note such an association. Differences in intakes of energy and protein may alter the animal's ability to deal with cancer cells; animals deficiency in protein and aminoacids may enhance tumour-inhibitory cellular immunity by reducing "blocking" humoral factors. Excess of retinoids and deficiency of riboflavin exert anticarcinogenic activity, whereas deficiencies of lipotropic factors, iodine and magnesium may enhance the growth of certain tumours. The mechanisms by which such dietary changes exert their effects on cancer are not clear; altered immunity function, restriction of available nutrients, changes in cell-surface proteins and enzymes, etc. may be important.

In man, three major types of dietary alterations have been postulated to be linked with the occurrence of cancer. One, some types of tumours occur more frequently in association with nutritional deficiency states; e.g. carcinoma of the cervix and vitamin A deficiency, carcinoma of the esophagus in association with iron deficiency anemia and Plummer-Vinson syndrome, large amounts of carbohydrates with ?lower intakes of vitamin C and gastric cancer. The role of alcohol in the genesis of malignancy is probably secondary; it has been linked with carcinoma of the larynx and upper GI tract in heavy smokers and with liver tumours. Two, some tumours occur in higher frequency in the obese; eg. endometrial and renal carcinomas. There may be some dietary factors contributing to the genesis of bladder and breast cancers. It has been postulated that a low fibre diet predisposes to colonic cancer by causing fecal stasis, the increased transit time allowing longer contact with dietary carcinogens, bacterial growth and conversion of bile salts into potential pathogens. Three, food additives and contaminants, eg mycotoxins such as aflatoxin, and diethylstilbestrol, may increase the frequency of cancer.

Primary intestinal lymphoma has interesting geographic distribution. In developing countries, it occurs 2-3 decades earlier in life than in industrialized countries, and the preferential site of its occurrence is different. It may be associated with alpha chain disease, which has been postulated to result from continuous antigenic stimulation of IgA producing cells in the lymphoid tissue of the gut. A correlation between animal protein consumption and lymphoma mortality has also been reported. The concept of enhanced absorption of harmful antigens leading to tumours is supported by the higher frequency of cancer in celiac disease.

Genetic susceptibility and other environmental factors such as contamination of food with oncogenic viruses may play critical role, however there is little data in this area.

Another facet of nutrition-cancer interaction is the frequent occurrence of nutritional deficiency secondary to cancer, and this may lead to immunodeficiency and higher incidence of infections, as has been shown for lymphomas and leukemias.

NUTRITION AND AGEING

There are several facets of interaction between nutrient intake and the process of ageing. The major health problems of old age are infections, cancer and atherosclerosis, each of which is influenced by nutrition.

The common clinical manifestations of the majority of old individuals - loss of subcutaneous tissue, cachexia and anemia - resemble those of undernourished children. The syndrome of progeria or premature senescence bears a striking resemblance with some of the clinical features of marasmus. Recent nutrition surveys in Canada have shown the frequent presence of nutritional deficiencies in senior citizens. It is possible that nutritional imbalance contributes to the progressive decline in many biological functions in old people. There is a significant impairment of immunological responses, and nutritional deficiencies may underlie such a reduction in immunocompetence. These immunologic changes may play a role in the genesis of life threatening infectionn with a number of pathogens of variable virulence. There is evidence that with advancing age, there may be an imbalance between the activity of different components of the immune system, eg cell-mediated and humoral immunity. These alterations, perhaps nutritional in origin, may determine the susceptibility to develop autoimmune diseases and malignancy.

In experimental animals, there is good evidence to support the relationship between dietary intake and longevity. In some genetically immunodeficient mice, mild to moderate undernutrition decreases the frequency of pathologic diseases, delays the onset of autoimmune processes and prolongs life. In animals allowed free access to food in terms of quantity and quality, the amount of energy intake and consumption of proteins and carbohydrates correlates with increments of growth and life span.

On the other hand, ageing is associated with changes in appetite, metabolism and nutritional requirements. This will necessitate new approaches to feeding the elderly to keep metabolic homeostasis. There is need for the quantitation of adequate and safe allowances to support

body's repletion of nutrients during and after stressful stimuli and to maintain maximum resistance to disease.

Finally, there is the possibility of a link between genetic-metabolic factors and nutrient intake over several years in the causation of atherosclerosis. Such an influence of dietary factors is likely to have its origins in early life. Both the quality and the quantity of dietary constituents may be important determinants. Interestingly, many patients with fatal ischemic heart disease have high titers of antibodies to common food protein antigens, an observation also made in undernourished subjects. The production of food antibodies is facilitated in the presence of impaired mucosal immunity.

Other diseases of old age may also be linked to nutrition. These include osteoporosis, peridontal disease, diverticulosis, hemorrhoids and varicose veins, and colonic cancer. The pathogenesis of these disorders is multifactorial and dietary influences over several years may contribute to an increased frequency. However, the epidemiological data in this area is not firm.

NUTRITION AND GASTROINTESTINAL DISORDERS

Nutritional deficiency is associated with a number of structural, biochemical and functional alterations of the gastrointestinal tract, pancreas and liver. In kwashiorkor and marasmus, the salivary glands are atrophied initially, with shrinkage and degranulation of the enzyme-secreting cells. Mucus producing cells are relatively unaffected. Amylase activity is reduced. In adults and in some children with malnutrition, the parotid glands hypertrophy and become prominent clinically. The jejunal mucosa shows varying changes of partial villus atrophy. Electron microscopy shows accumulation of lipid droplets in epithelial cells at the tips and sides of the villi, mainly in the apical cytoplasm. In marasmus, the changes are less pronounced, but there are abnormalities of the brush border, large autophagosomes and residual bodies, and the deposition of collagen filaments and a dense finely granular material below the basal lamella. These changes reverse to normal after nutritional recovery. The frequent association of malnutrition with changes in gut microflora and the common occurrence of infections, makes it almost impossible to attribute these morphologic changes to nutritional deficiency only. Functionally, varying degrees of malabsorption of fat and d-xylose, and of disaccharides have been reported. It is likely that nutrition-related absorptive defects would be more pronounced in those with a genetically determined deficiency, eg of lactase. In the few children studied, jejunal dipeptidases have been reduced, but absorption of amino acids using in vivo uptake techniques has been normal. The presence and contribution of any functional metabolic changes intrinsic to the enterocyte in malnutrition are not established. In the ileum, villus atrophy is associated with impaired vitamin B 12 absorption and macrocytic anemia.

Pancreas is atrophic with disruption of acinar pattern and diminution of secretory granules and organelles. Pancreatic enzyme activity in the duodenal juice is reduced, trypsin being less affected than other enzymes. The volume and pH are normal. Mild abnormalities of pancreatic function may persist for several months to years after nutritional rehabilitation.

The liver shows an increase in fat, probably a direct result of failure to transport triglycerides out of the hepatocyte because of reduced lipoprotein synthesis. Biochemical evidence of liver cell dysfunction occurs in a few malnourished subjects, and is a bad prognostic sign. The probable contribution of malnutrition to liver damage has been recently highlighted by observations on patients receiving intravenous hyperalimentation and in those undergoing bypass operations as treatment of morbid obesity. It must be pointed out, however, that the ecosystem that breeds

malnutrition also increases the risk of exposure to potential hepatotoxins, both biological and chemical.

These alterations in the structure and function of the gastrointestinal tract, pancreas and liver, in malnutrition contribute to the increased frequency and severity of diarrhoea. The episodes are more prolonged and difficult to manage.

NUTRITION AND GROWTH

There is little doubt that the fundamental effect of nutritional deficiencies is on cellular regeneration and protein synthesis, and that these basic changes underlie the consistent growth failure in undernourished individuals. The extent and the nature of growth failure, ie weight loss, short stature, etc. is governed by the magnitude and timing of nutritional deficiency, and the presence of aggravating factors such as infection. If growth failure occurs in utero, "catch up" increments are usually not adequate, so that permanent alterations in size may occur. Since short stature is a recognized predisposing factor for low birth weight of the offspring, this sets up a vicious circle. Similarly, nutritional deprivation during most of the periods of rapid growth, ie infancy and prepubertal, may be more deleterious for growth, than deficits during periods of relatively slow growth. It is likely that these intergenerational effects of nutrition on growth are part of the explanation for the ethnic-geographic variations in anthropometric measurements.

NUTRITION AND CARDIOMYOPATHY

In selected nutritional deficiencies, myocardial dysfunction may occur, eg thiamine deficiency. This may be fatal unless recognized and treated in time. In some developing countries with rampant malnutrition, there is a high frequency of obscure cardiomyopathies; the interaction of infectious agents and nutritional deficiencies may be important in the pathogenesis of these syndromes.

NUTRITION AND OSTEOPOROSIS

Bone changes are frequent manifestations of deficits of protein, calcium and vitamin D. Often, osteoporosis is one of the major manifestations of malnutrition. Permanently disfiguring malformations of the bones may occur. Pelvic changes may create difficulties during labour and higher rates of stillbirth and birth trauma.

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NUTRITION, MALNUTRITION, AND DISEASE:

A SOCIAL SCIENCE PERSPECTIVE

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Background Paper for the Workshop on Nutritional Intake and Disease Response, Hyannis, Massachusetts, September 25-29, 1978.

NUTRITION, MALNUTRITION, AND DISEASE:

A SOCIAL SCIENCE PERSPECTIVE

by John Osgood Field

Studies of nutrient intake and disease response (conventionally known as "nutrition and infection") fall into three general categories, as suggested in Figure 1.

Figure 1: The Nutrition-Infection Connection: Three Foci for Research

Research Foci	Core Questions
1. The interplay of nutrient intake with the type, prevalence, and severity of disease	1. What are the dynamics at work?
2. The functional effects of malnutrition	2. What do these dynamics mean for both individual and society?
3. Policy responses	3. What can be done about the problem? More precisely, what works, under what conditions and why? Also, what do different options cost?

If this is a fair accounting, two observations follow. First, the subject matter -- to a surprising extent perhaps -- is interdisciplinary. Technical specialists may dominate the analysis of nutrition-infection dynamics; but when the focus shifts to the functional implications of

AUTHOR'S NOTE

My assignment is to write about food intake and disease response from a social science perspective. This is akin to asking an astronomer to sound intelligent after peering through a microscope. One has the uncomfortable feeling of a disciplinary mismatch -- protozoa and paramecia not being the stuff of which galaxies are made -- and something of a macro-micro mismatch as well. "Functional competency," however specified, is probably best studied by meticulous observation of individual cases. A behavioral scientist with knowledge of nutrition, medicine, or both might be up to the task; not so a political scientist whose limited forte is with broad-gauged patterns and processes. Central casting may have made a mistake.

Moreover, my sense is that no "state of the art" concerning nutrition and infection exists in social science. At least I know of none. Nor do I know of any social scientists who might claim otherwise. There may be doctors and nutritionists with an acquired wisdom concerning social systems (Wray, Navarro, Scrimshaw, and Mayer, among others, come to mind). The reverse does not hold, however. What social scientists know about the food-health nexus is extremely limited, strictly non-technical, and in no way professional. If I am correct, then it follows that the social scientist is largely irrelevant to the definition of a research agenda concerning intake and disease. A glimmer of relevance may reside in his natural tendency to look for the applications of knowledge to policy and to raise the banner of practical significance lest scientific inquiry turn totally inward.

This is a thin reed on which to write a paper. Honorably, if not wisely, I have -- by and large -- resisted the temptation to stray from the topic onto more comfortable ground. The result may fail to satisfy. However useless substantively, this paper may at least provide a framework for discussion.

John Osgood Field
Medford, Massachusetts
September 11, 1978

this interplay, they are soon joined by behavioral scientists, cultural anthropologists, economists, and others. With an invocation to policy and design of interventions, the canvas broadens to include health administrators, social workers, even (God forbid!) political scientists. Something which at first blush seems coherent, manageable, and rigorously scientific quickly becomes anything but. One suspects that the current state of knowledge is neither cumulative nor additive as a result.

Second, as one moves from the first research focus to the second and from the second on to the third, a rapid decline in expertise occurs. In part, this is because knowledge about nutrition and disease logically begins with research on nutrition and disease. Everyone else gets into the act rather later in the game, as the growing body of core knowledge invites horizons to expand. The three foci, therefore, represent concentric circles, with each wider circle following upon the one before. Moreover, the move outward entails a sharp diminution in scientific purity. The relatively straightforward testing of relationships at the "micro" level gives way to a profusion of influences at work at more "macro" levels of analysis, where concepts are increasingly fuzzy and difficult to measure and where the necessary data are typically either unreliable or non-existent. For these reasons, the "state of the art" may be expected to remain most developed, for some time at least, where it was initiated, in the laboratory and under conditions of well-controlled field experimentation and observation.

This paper will comment briefly on each research focus and attempt to identify issues for further investigation.

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Research Focus #1: The Dynamics of Nutrition, Infection, and Nutritional Status

Three general points seem to be well established concerning this critical set of relationships on which all else depends:

1. Food intake and the presence or absence of infectious disease are the two principal determinants of nutritional status. Malnutrition, as a departure from nutritional adequacy on the deficit side, is an outcome condition reflecting some combination of inadequate consumption and impaired biological utilization of ingested nutrients by the body. Granted that malnutrition has a complex etiology that is often very difficult to specify, ultimately it is the interplay of "nutrition" and "infection" which dictates a person's nutritional status.[1]

2. Inadequate intake of food and impaired biological utilization due to infection are typically found together in malnourished subjects, especially those in the most vulnerable age cohort of 6 - 36 months. A poor diet weakens the body and reduces resistance to disease, while infections result in nitrogen loss, depletion of tissue protein, depressed cell-mediated immunity, and anorexia. The two principal determinants of nutritional status, therefore, are interactive to a significant degree.

3. The effects of inadequate intake and repeated health insults are synergistic. Not only do infections make malnutrition worse while poor nutrition increases the severity of infectious disease.[2] Their interaction "is more serious for the host than would be expected from the combined effect of the two working independently."[3] Each intensifies the implications of the other, and it

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[1] For example, see the model of malnutrition causality in F. James Levinson, Morinda: An Economic Analysis of Malnutrition Amoung Young Children in Rural India, Cornell-MIT International Nutrition Policy Series, 1, 1974, p. 6.

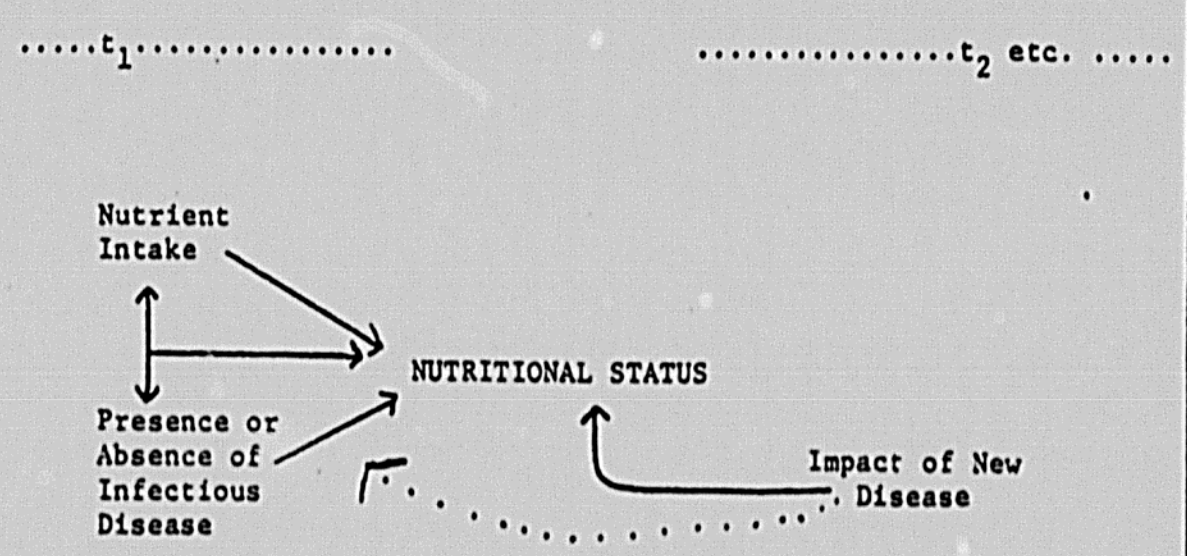
[2] Michael C. Latham, "Nutrition and Infection in National Development," in Philip H. Abelson, Food: Politics, Economics, Nutrition and Research (Washington, D.C.: American Association for the Advancement of Science, 1975), p. 69.

[3] Nevin S. Scrimshaw, "Nutrition and Infection," Progress in Food and Nutrition Science, 1 (1975), p. 394.

is this negative synergism which produces growth failure and which underlies much infant and early childhood mortality.[4]

In essence, research on nutrition and infection first examines the way in which the two together interact to produce variation in nutritional status. It then addresses the significance of new health insults for further changes in nutritional status.[5] "Infection," therefore, is related both to "nutrition" and to "nutritional status" in the manner of Figure 2.

Figure 2: Dynamics of Infection, Nutrition, and Nutritional Status



[4] See, for example, John B. Wyon and John E. Gordon, The Khanna Study: Population Problems in the Rural Punjab (Cambridge: Harvard University Press, 1971) and Ruth Rice Puffer and Carlos V. Serrano, Patterns of Mortality in Childhood (Washington, D.C.: PAHO-WHO, 1973).

[5] That miserable child in Santa Maria Cauqué whose growth failure in response to repeated health afflictions has become an international reference is a case in point. See Leonardo J. Mata, "The Environment of the Malnourished Child," in Nevin S. Scrimshaw and Moises Behar, Nutrition and Agricultural Development: Significance and Potential for the Tropics (New York: Plenum Press, 1976), pp. 52-3.

Without question, Research Focus #1 is the strongest of the three research foci in terms of effort made, findings reported, and confidence derived. Even so, the experts talk of untested theory, observed exceptions, inconsistencies, and gaps in knowledge.

Perhaps what appears on the surface to be a fairly straightforward pattern on nutrient intake and disease response in which they vary positively (the more, the better; the less, the worse) is much more complex. Perhaps, too, the impact of new disease on nutritional status is highly variable. It may be worth hypothesizing that these relationships differ significantly -- and not necessarily in linear fashion -- across types of nutrient, types of disease, degree of nutrient deprivation, and severity of health insult. Obviously this is as far as a social scientist can really take the subject, but it suggests that much useful work remains to be done at the core of the concentric circles.[6]

Research Focus #2: The Functional Effects of Malnutrition

As an outcome condition reflecting inadequate food intake and infectious disease, malnutrition -- in turn -- has functional implications for those experiencing it which are observable at both micro and macro levels of analysis. At least some of these implications are summarized in Figure

[6] Many attending the Hyannis workshop may be inclined to accept this statement as an obvious truth and accordingly devote considerable attention to the research called for. It might be more appropriate -- or in any event challenging -- to treat this statement as a hypothesis only, one to be defended against an alternative hypothesis to the effect that another round of studies on nutrition and infection will do no more than confirm the obvious yet again and leave researchers making intellectual mountains out of practical molehills.

3 below. Individually and together, they indicate why malnutrition has become such a developmental cause celebre.

Figure 3: Malnutrition as an Outcome Condition and as a Barrier to Development

Inadequate Food Intake

- Quantity
- Quality

Impaired Biological Utilization (Digestion, Absorption, Metabolization) of Ingested Nutrients due to:

- Diarrhea, gastroenteritis, dehydration
- Respiratory infections
- Parasitic infestation
- Other health insults (fever, coughs, epidemics)

MALNUTRITION

Child Development

- Low birth weight (from maternal malnutrition)
- Physical stunting/blindness
- Reduced resistance to disease
- Low social stimulation
- Withdrawal, reduced social competence
- Impaired learning
- Reduced mental capacity (?)
- High mortality

Socio-Economic Development

- Low productivity, work efficiency
- Reduced capacity for change
- Unresponsiveness to family planning, high population growth rates
- Lower return on social sector investments (health, education, employment, etc.)
- Accelerated rural-to-urban migration (?)
- Threat to political stability(?)

A quick look at Figure 3 reveals that this research focus opens up a veritable Pandora's box of concerns, the precise parameters of which are not well established by any means but the general thrust of which is nonetheless quite clear. In terms of its effects, malnutrition ranks among the most pervasive and serious health problems in the world today. Protein-calorie malnutrition, in particular, results in physical stunting of the very young, impaired learning, possibly even irreversible brain damage, and -- of course -- high rates of infant and early childhood mortality. An indicator of under-development, extensive malnutrition is also believed by many to be a barrier to development, for it constrains human competence and productivity, inhibits a society's capacity for change, and serves as a powerful disincentive to the practice of family planning. Malnutrition does much to lock people into the very state of deprivation from which it is derived. Just as malnutrition is a key ingredient of the poverty syndrome, combating malnutrition is probably a necessary, if not sufficient, condition for breaking out of it.

So much for the glittering generalities. In fact, some of the effects imputed in Figure 3 are little more than plausible propositions on which little or no research has been done. In quite a few cases, research or no research, the precise role of malnutrition is extremely difficult to isolate. This is especially true at the macro level of socio-economic development, where so many factors come into play. Figure 4 summarizes the current state of knowledge concerning the functional implications of malnutrition. However crude, this summary demonstrates

[7] As indicated, Figure 4 is an interpretation only. It invites challenge.

Figure 4: The State of Current Knowledge Concerning the Functional Implications of Malnutrition -- An Interpretation

	The State of Knowledge			
	Established	Documented	Asserted	Unexamined
Child Development				
Low birth weight		X		
Physical stunting/blindness	X			
Reduced resistance to disease	X			
Withdrawal, reduced social competence[a]		X		
Low social stimulation			X	
Impaired learning		X		
Reduced mental capacity			X	
High mortality	X			
Socio-Economic Development				
Low productivity, work efficiency[b]		X		
Reduced capacity for change			X	
Unresponsiveness to family planning, high population growth rates[c]			X	
Lower return on social sector investments			X	
Accelerated rural-to-urban migration			X	
Threat to political stability				X

[a] Withdrawal is well established. Whether it really entails reduced competence in interacting with one's social (and physical) environment is less clear.

[b] These effects have been observed in certain labor-intensive enterprises. The case is not at all settled when, as is usually the case, individual work performance is less significant for total output. Nor is it clear that malnutrition in early childhood really results in poor work performance by adults.

[c] This is a hotly contested issue. However attractive, the "child survival hypothesis" is probably flawed in its logic. The evidence to date is indirect in any event.

the pronounced difference between what is known or even documented at the individual and societal levels. It also suggests that, overall, the state of knowledge is not especially advanced.[8]

One thing that Figure 4 does not do is discriminate between the effects of mild, moderate, and severe PCM. Indeed, quite possibly most of what is claimed about the consequences of malnutrition generally, here and elsewhere, pertains solely or in large measure to the severe manifestations of it. Of course, the more serious the malnutrition, the clearer the case and the greater the dramatic effect. Two things happen at the moderate and mild portions of the continuum: much of what is asserted is either patently false or at least questionable, and research attention fades significantly.

Joy[9] and others believe that the time has come for research to examine the implications of mild and moderate malnutrition much more specifically and concertedly than in the past. This makes very good sense if only because most malnutrition among vulnerable groups is not severe. Perhaps the dynamics linking nutrition and infection are quite different, in nature and in outcome, when the deficits in food consumption are small. Perhaps, too, the effects of additional disease on an existing state of malnutrition are also much less serious when the malnutrition is mild.

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[8] Again it may be worth putting forward a revisionist view, that more research knowledge will only confirm knowledge derived from other sources: the senses, logic, experience, intuition. The latter are not scientifically respectable, to be sure; but in practical terms they may be enough, especially at the more cacophonous macro levels of analysis.

[9] Leonard Joy, "Research into Intake and Function," PAG Bulletin, VII (1977), pp. 50-52.

Some scholars believe this to be the case.[10]

Moreover, there may well be as yet unknown threshold effects or disease-specific effects, knowledge of which would permit a more functional classification of malnutrition than is now possible.[11] Perhaps, as Leonardo Mata argues, estimates of the prevalence of malnutrition based on weight-for-age measurements and the Gomez classification are seriously inflated and that physical stunting, in itself, should not be considered malnutrition.[12] If Mata is right, particularly on the latter point, then it might be possible to target nutrition interventions more precisely and with greater overall cost-effectiveness than is now being done.[13]

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[10] For example, Dr. S. G. Srikantia, Director of the National Institute of Nutrition in Hyderabad, India, has hypothesized that the synergistic relationships between nutrition and infection become pronounced only at relatively low nutritional levels. (Personal communication to Davidson R. Gwatkin referred to in Gwatkin's paper, "Nutrition Planning and Physical Well-Being in Kerala and Sri Lanka," Overseas Development Council, January 1978, p. 19.) Positive and negative evidence based on specific relationships is reviewed in Jon Eliot Rohde, "Preparing the Next Round: Convalescent Care After Acute Infection," position paper for the National Academy of Sciences, Food and Nutrition Board, Workshop on Effective Interventions to Reduce Infection in Malnourished Populations, 13-16 June 1977.

[11] Joy called for a functional classification of malnourished populations more than five years ago (Leonard Joy, "Food and Nutrition Planning," Journal of Agricultural Economics, XXIV (January 1973), 22 pp. as IDS Reprint #107). See also Doris H. Calloway, "Functional Definition of Nutritional Status," PAG Bulletin, VII (1977), pp. 53-58.

[12] Leonardo Mata, "The Nature of the Nutrition Problem," paper presented at the International Study Symposium on Policy Making and Planning to Reduce Malnutrition, The University of California at Berkeley, Berkeley, California, March 29-April 1, 1977, 34 pp.

[13] The more precise the targeting the better according to Shlomo Reutlinger and Marcelo Selowsky, Malnutrition and Poverty: Magnitude and Policy Options, World Bank Staff Occasional Papers, No. 23 (1976), chapters 3 and 4.

Two final points may be made regarding the implications of malnutrition, both of which refer to the connection between this research focus and the other two indicated in Figure 1. First, it is helpful to keep in mind the strong likelihood that the functional effects of malnutrition on the individual (and, by aggregation and inference, on society at large) depend critically upon the dynamic interplay of different kinds and degrees of nutrition, infection, and nutritional status. As long as this remains a valid hypothesis, research on functional effects will itself be dependent, to some meaningful extent, on knowledge produced concerning the basic dynamics. If so, Research Focus #2 assumes continued guidance from Research Focus #1.

Second, Research Focus #3 on policy responses to malnutrition should rest, in part at least, on both of the others. The dynamics produce outcomes which either are or are not serious in their implications. The thrust of research on policy and interventions is bound to be on how best to impact malnutrition at acceptable cost. However, a prior issue is what forms of malnutrition should be addressed and at what degrees of severity. The answers here depend on Research Focus #2 as informed by Research Focus #1. Ideally, the third focus is the least autonomous, as well as the least scientific, of the three. Whether this is the case, in fact, depends on the flow of knowledge across the concentric circles, which -- in turn -- depends on the willingness of scientists, social scientists, and programmers to interact with one another.

Research Focus #3: Policy Responses

Nutrition programs of one description or another may be found in most countries, at times in bewildering profusion. Nutrition planning is very much more rare, but this new field promises to introduce greater conceptual order and methodological rigor to nutrition interventions while possibly also upgrading their importance in the development efforts of low income countries. Every country has a health ministry, of course, although most people in most countries receive little, if any, modern health care. What should research do under these circumstances?

One thing which should be done is being done. That is taking stock of experience. At Harvard, CARE, the World Bank, Community Systems Foundation, and elsewhere serious efforts are being made, at last, to examine what has been attempted, where and how, and to estimate effectiveness in relation to costs. In the main, the documentary evidence concerning nutrition programs and specific interventions is long on description (although good case studies are rare), adequate - if unsophisticated - on costs, weak on impact, and limited on process.[14] All of this suggests some lines of fruitful research.

One line of special pertinence to the nutrition-infection nexus concerns the role of the health sector in addressing malnutrition. Many nutrition interventions are health related, in fact, while a country's health infrastructure is often employed for transmission of supplementary foods, nutrition education, and related services to those believed to need them. For their part, many health interventions - curative and preventive also have a direct bearing on nutritional status through their impact on the incidence and severity of disease. Effective action against the morbidity problems at early childhood is an appropriate

[14] For example, less than a quarter of the nutrition programs all over the world reviewed by the Harvard Institute of International Development reported having analyzed data on nutritional status.

means for impacting malnutrition as well. If the core problem - the interaction between inadequate nutrient intake and lowered disease response - is a negative synergism, one approach to its solution suggests itself in the potentially positive synergism of nutrition and health interventions. Health systems, in short, merit invigorated attention.

If so, we are faced with a curiosity. On the one hand, in most low income countries malnutrition - once recognized - is defined as a health problem, with the health sector given principal responsibility for dealing with it. On the other, the explosion of intellectual interest in malnutrition has been accompanied by an almost studied neglect of the health sector as a means of doing so.[15] Indeed, the recent enthusiasm for multi-sectoral nutrition planning has received at least some of its momentum from a conscious desire to escape from the imputed parochialism of the medical approach to the problem. Health specialists may be displaying a new-found interest in malnutrition,[16] but nutrition specialists have shown little programmatic interest in health.

This not-so-benign neglect makes no sense. In the first place, as Ivan Beghin puts it so well, "Nutrition cannot be separated from health, and any nutrition programme will possess a very heavy health component. Pure nutrition is out, hopefully forever."[17] No one seized

[15] To illustrate, Alan Berg's seminal book, The Nutrition Factor, contains virtually nothing on health care delivery as an approach to improving nutritional status.

[16] The World Bank, Health: Sector Policy Paper (Washington, D.C.: The World Bank, 1975).

[17] Ivan Beghin, "Improving Nutrition at the Local Level," Carnets de l'enfance, 35 (July-September 1976) p. 18.

with the seriousness of the malnutrition-morbidity-mortality syndrome could possibly disagree. Even when the malnutrition is mild or moderate, health care is often the most appropriate response, in addition to being the only operationally feasible response. Indeed, the time may have come to begin liberating the problem of malnutrition from the protective embrace of nutritionists in order to emphasize the instrumental role of people responsible for health care delivery.[18]

A second reason why the neglect of health care delivery makes no sense concerns the rather ambiguous track-record of multi-sectoral nutrition planning itself. This approach is, understandably, held up as the most appropriate response to the complexities of malnutrition since it seeks to harness the resources and capabilities of different ministries behind a coordinated plan of action. Unfortunately, however, multi-sectoral nutrition planning remains more an ambition than an achievement.[19] In many low income countries, most in fact, it might be premature and counter-productive to push it. At this stage much can be done within established

[18] This suggestion will not be met with favor by many. It is based, in part, on personal experience in a country where the Minister of Health, a well-intentioned surgeon, wanted his ministry to do something about malnutrition, did not know what could or should be done, and formed a committee of distinguished nutritionists to advise him. The result was a lot of words and no action, with everyone waiting for the Minister to produce funds so that he might get some for his own pet projects, typically entailing research. And this in a country with an unusually well disseminated health infrastructure capable of reaching people in need. The Minister's mistake, now being rectified, was to assume that, if malnutrition is the problem, nutritional expertise must be the solution, a one-to-one relationship as it were. It simply did not occur to him at the time to call upon the specialists in his own ministry responsible for conventional health care services. He is now doing so.

[19] See page 15 for this note.

spheres of competence, particularly health, without requiring a formidable amount of administrative engineering as a precondition. "Sectoral review" may well be a more realistic first step in confronting malnutrition, with analysis of the health and agricultural sectors assuming a logical

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[19]We should no longer be surprised that this is so. The multi-sectoral approach to nutrition planning suffers from at least three major flaws.

1. It is predicated on the willingness of governments to give reasonably high priority to malnutrition as a problem calling for direct policy intervention and to set up strong planning and executive institutions for this purpose. The required level of commitment rarely exists, and established sectors (agriculture, health, education, etc.) typically have other priorities.

2. The approach assumes an abundance of accurate data and a wealth of disciplinary and inter-disciplinary expertise combined with detailed familiarity with conditions in the country. It also assumes both the hardware and methodological skills necessary to convert all this information into cost-effective decisions.

3. The approach assumes that even modest financial allocations, when combined with sophisticated planning techniques, will result in policies and interventions that successfully impact the problem regardless of anything else that may be true about the economy and polity, other policies being pursued, the overall pattern of development, and the control over resources in society.

Multi-sectoral nutrition planning, in short, is a nice idea that may not work. It is both too broad and too narrow, too broad because of its cross-sectoral ambitions and because governments rarely harness total systems behind nutrition goals, too narrow because nutrition is seldom isolated as an exclusive focus of social sector programming. Indeed, in its pristine form the multi-sectoral approach reflects the Western cult of rationality. Although designed for underdeveloped countries, it seems to forget that they are underdeveloped in data and in planning and management skills, to say nothing of the resources necessary to undertake a comprehensive assault on malnutrition. The multi-sectoral approach is unbelievably demanding. All too often it is politically naive, while also being inattentive to problems of implementation and insensitive to the wishes of its intended beneficiaries. Even at its best, multi-sectoral nutrition planning runs the risk of being more intellectually elegant than functionally practical. It also runs the risk of being coopted -- and corrupted -- by basically conservative governments unwilling to address the structural constraints on popular well-being.

priority.[20]

Not only are we faced with a curiosity; we are faced with a dilemma. If health systems have a logical relevance to malnutrition and if they are also among the better disseminated structures available to the governments of poor countries, the fact remains that most health care delivery is deficient. Not only is this so when services are matched against needs; it is also the case when services are matched against proclaimed objectives. All too often, ministries of public health provide little effective public health delivery.

There are good reasons for this performance gap, of course. Health systems typically function under a number of serious handicaps.

- Politically, health ministries are among the weakest in most governments. Every country may feel it necessary to have a health ministry, but in rather few countries is health a high political priority. In many instances, allocations to health are seen as competitive with allocations for development, and the latter prevail.
- Health ministries are often among the most poorly administered as well. Doctors rarely make good administrators, yet the medical profession dominates most health systems.

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[20] Nutritional impact of government policies is one of the foci for research recommended by Study Team 9 ("Nutrition") of the National Academy of Sciences' World Food and Nutrition Study (Vol. IV: Supporting Paper, Washington, D. C.; 1977, pp. 50 - 60). See also James M. Pines, "The Impact of Nutrition Goals on Agriculture," Food and Nutrition, 2 (1976), 2 - 4.

- The training of medical elites, often outside their own country, gives them a perspective on medicine far removed from the health needs of the great majority of people in their society. Younger doctors are similarly educated to skills and values that lack relevance to majority needs.
- Health infrastructures are usually top-heavy as a result. Pride is taken in big city hospitals with the latest modern equipment, while rural health service suffers from low prestige, insufficient funding, poor staffing, and a host of morale problems. For the individual doctor, economic incentives accentuate the urban bias that exists.
- Penetration of the rural (and urban slum) periphery of low income countries is extremely difficult organizationally and logistically.
- Even where formal structures exist, rarely do they achieve real impact on health problems within their jurisdiction. System-society interaction is often a seriously deficient final link in health care delivery. The irony is that health centers can be both overburdened and underutilized at the same time.

In sum, outreach is limited, popular participation in modern health care is low, and the capacity to produce change is - all too often - very disappointing. Most health systems are notoriously cost-ineffective. Moreover, they are typically weakest in those respects where the need for them is greatest: in addressing malnutrition, morbidity, and infant and early childhood mortality.

Much needs to be done to turn this unhappy situation around. As an increasing number of governments give more attention to rural development and seek a better balance between equity and growth while also attempting

to achieve breakthroughs in family planning, the importance of population-based health care delivery is likely to increase considerably. Health status, nutritional status, mortality, receptivity to family planning, and productivity are all related in ways that bring health services into the mainstream of a country's development efforts instead of being on the fringe. Indeed, far from being irrelevant or only distantly relevant to development, ministries of health can be among the foremost participants in helping the process along. For ministries of health are uniquely positioned to attend to both elements of the demographic transition: births and deaths. As the best conveyor belt for disseminating family planning information and technology in society, they potentially play a frontal role in the implementation of population policy. More to the point, as the agency most immediately responsible for public health, including malnutrition, they are essential to a focused attempt to bring infant and early childhood mortality down. It comes as no surprise that those countries which have given priority to equity-oriented rural development (such as China, Taiwan, South Korea, Sri Lanka, Cuba, and Tanzania) have done the most to redirect and upgrade their health services.[21] They also tend to be the countries which have made the most substantial gains in combating malnutrition, lowering mortality, and reducing population growth.[22]

By and large, research on health care delivery is still conducted by members of the medical profession. Rather little has been done by social scientists, and inter-disciplinary "team" research also remains

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[21] The same applies to the Indian state of Kerala.

[22] See, for example, William Rich, Smaller Families Through Social and Economic Progress, Overseas Development Council, monograph no. 7 (January 1973), 77 pp; John W. Ratcliffe, "Poverty, Politics, and Fertility: The Anomaly of Kerala," Hastings Center Report (February 1977), 34 - 42; and Gwatkin, op. cit.

rare, although some recent initiatives look promising. The research bias, like that of most health systems, is reflective of an orientation which sees needs and problems in largely technical terms and which, accordingly, prescribes largely technical solutions to them. However valid, this thrust entails a number of distortions which can be serious. For example, when basic problems facing a health system are perceived as internal to that system, very little attention is given to how the system interacts with the society of which it is a part. The latter realm is beyond the usual analyst's competence or mandate, but it is often critical in improving the performance of a health system.

The following research topics are responsive to old needs and new opportunities. They are listed here in outline form for the sake of brevity.

1. Impact

Inasmuch as the purpose of health (and other) interventions is to improve nutritional status, it is sobering to realize how little is really known concerning the impact of the many things going on, somewhat ritualistically, all over the world. At least with regard to PCM, the core policy question identified in Figure 1 - what works, under what conditions, and why? - remains substantially unanswered.[23]

A priority need, therefore, is to analyze and document the impact achieved by alternative types and combinations of interventions in different settings. Wherever case experience permits, we simply must go for the

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[23] Incredible as it may sound, Carl E. Taylor and his colleagues were quite justified in making the following statement based on their work in Narangwal, Punjab, India. "Nutrition care can increase significantly the weight and height of total populations of children. As far as we can determine, this is the first controlled experiment of total child populations under natural conditions where this has been demonstrated" (The Narangwal Nutrition Study, Report to the World Bank, November 1977, Paper III: p. 28).

jugular and ask: given what has been done, what difference has it made? The effectiveness side of cost-effectiveness requires a great deal of attention, if only to establish whether and when so-called nutrition interventions are - and are not - an appropriate response to malnutrition.[24] Given the importance of the health sector, impact studies might usefully focus on alternative modes of health care delivery.

2. Process

Although rarely addressed by technical experts, how programs are implemented is often a critical determinant of their success. The process effects the outcome. How well what is provided works depends, in part, on how it is provided. Research is needed on the operational characteristics of nutrition interventions and equally on how people in the targeted population respond to what, in essence, are attempts to manipulate them.[25]

Two themes relevant to health care delivery will illustrate. One has to do with system-society interaction, the other with surveillance. Concerning the former, health delivery succeeds or fails in direct proportion to how people in society relate to the health system.[26]

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[24] The author is presently engaged in a longitudinal analysis of more than 4,000 growth charts and data concerning health, family history, socio-economic status, environment, and intervention inputs from Kanyakumari District, Tamil Nadu, in India. When completed, this study should enable us to say several things about impact: to what extent it has been achieved and on whom, at what degrees of PCM, in the context of what health complications, under what family and economic circumstances, where, and in response to what. The last refers both to nutrition/health services and to broader attempts at socio-environmental engineering. More analyses of this kind would make a significant contribution to operational knowledge, especially when examining real programs that are replicable.

[25] An illustration may be found in John Osgood Field, "Development at the Grass Roots: The Organizational Imperative," paper presented at the World Food Forum: Practical Points of View, Hiram College, Hiram, Ohio, March 31, 1978, 35 pp.

[26] This observation is developed poignantly in D. Banerji "Health Behaviour in Rural Populations: Impact of Rural Health Services," Economic and Political Weekly (December 22, 1973), 2261 - 2268.

Most health systems in low income countries appear to function in ways detrimental to their mission. A major part of the problem lies in a cluster of socio-cultural variables influencing the recruitment, socialization, and operational orientation of medical personnel at the local level where contact with the population takes place. At the same time, there is evidence to suggest that popular receptivity to modern health care is largely indifferent, if not negative, and that utilization rates are low. Inconvenience is one reason for this hiatus between system and society. Professional and class arrogance is another, and mutual misperception is a third. Unfortunately, very few studies address health care delivery from a sociological and attitudinal perspective. Given the importance of this dimension, more work is needed quite urgently, if only to enable existing health systems to function more effectively in their environments.

Surveillance is a relatively new interest, and it is an important one. The National Nutrition Program in the Philippines, China's barefoot doctors, the mini-posto system in Brazil, and India's anganwadis - to mention but a few cases - are attempts to monitor health and nutritional status in village communities using designated local people as the key agents of problem identification and then solution. The objective is to identify persons at risk, children especially, and to tend to their needs before their situation worsens and the cost of treatment increases. As an "early warning mechanism," surveillance is both a means of achieving outreach and the beginnings of a referral system. It is an attempt to blend preventive with curative medicine and to bring the latter to the very people who typically receive the

least of it. Because surveillance relies heavily on paramedical personnel, it requires sensitive recruitment, suitable training, and strong administrative reinforcement and support. Very little is known about any of these facets.[27]

[27] Surveillance is an idea that has received more exhortation and formal prescription to date than operational analysis. The need for research on the latter is underlined by Jon Rohde's very challenging ideas concerning the vital role of the mother in monitoring her own children in village settings (op. cit.). For any surveillance scheme - whether pre-illness or post-treatment - to work, there are several operational requirements. The village health worker (VHW) must:

1: Know how to detect problems (knowledge) ;
2: Actually do so - i.e., effectively monitor the population (conduct);
3: Be in a position to provide personal help (knowledge-materials) or to refer people to a higher level (that is, there must be an established system);
4: Actually do so.

The "at risk" family must then:

1: Accept the judgement of the VHW concerning the problem;
2: Act upon his or her advice.

If this entails referral or the delivery of services, the system must then:

1: Fulfill the promise of the VHW by responding effectively to the problem.

Moreover, all this must be at acceptable cost to the system and to the "at risk" family. This is what has to happen. How it is to happen is something else again. Neither aspect is well-understood. For some interesting thoughts on the subject, see John H. Bryant, "Community Health Workers: The Interface Between Communities and Health Care Systems," WHO Chronicle, 32 (1978), 144 - 148.

3. Health Dynamics

Health status (including nutritional status) depends not on health care delivery alone but on health care delivery in relation to a vast range of socio-economic and environmental conditions. This is well understood medically - the agent-host-environment triad - and historically, particularly with reference to the dramatic decrease in infant mortality in Western countries over the past 100 years or so. However, in a macro sense health dynamics are not at all well understood in low income countries, where health budgets are often competitive with resources for development.

A very useful role for research, therefore, would be to relate indices of health status - especially malnutrition, infection, and mortality (along with fertility) - to indices of general socio-economic development, on the one hand, and to indices of health care delivery, on the other, in the manner of Figure 5. Such an approach would indicate how responsive malnutrition and various types of infection are to different forms of development in a country (e.g. rising incomes, urbanization, literacy acquisition, electrification, availability of purified water, women entering the paid labor force, etc.), quite apart from the effects of that country's health system. It would also reveal the ways in which and the extent to which the health system is having, or might have, independent effects of its own, given an established pattern of overall development.[28]

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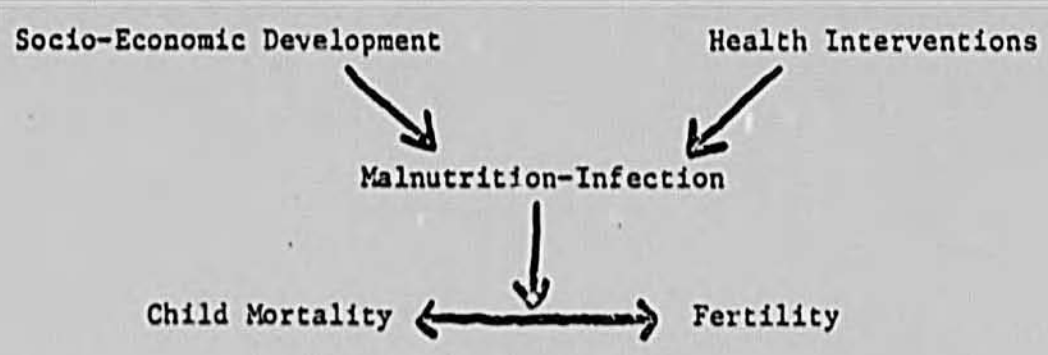
[28] To illustrate, using the simple model shown in Figure 5 and a body of data which is by no means exceptional, the M.I.T.-Cairo University Health Care Delivery Systems Project has unearthed a fascinating series of critical relationships (many quite unexpected) which have helped Egypt's Ministry of Health to understand better some of the health dynamics currently at work in Egyptian society and to identify the conditions in which its own services and programs are and are not having effect. In a related vein, the project has also examined variation in popular utilization of health facilities, again with some very interesting results. A third focus has been on the prevailing tendency, in Egypt as elsewhere, to under-record births and childhood deaths. (These studies are currently in draft form and will soon be available in a formal report. If interested, please contact the author for further information.) As a result of this work, the Ministry is beginning to view health problems not only in terms of medicine but in the context of development

Best Available Document

Figure 5: Health Dynamics in a Low Income Country



4. The Political Economy of Health Care

To a very significant degree, health systems reflect the socio-cultural, economic, and political environment of which they are a part.[29] What this often means is that health care delivery in poor countries is highly skewed spatially and socially, with urban elites having access to all the medical services they might require while the rural poor lack even the most rudimentary attention to their very real, immediate, and often pervasive health needs. Health services are not only maldistributed, they are structurally and functionally distorted as well. Hospitals with over-trained staffs and sophisticated equipment are favored over small, simpler, and more dispersed facilities utilizing paramedicals. Curative medicine is practiced at the expense of preventive health care. A clinical bias inhibits attempts at outreach and widespread coverage. Initiative for attention to health needs is left with the public, while the system remains passive. In general, such health systems may do justice to the standards

[29] Vincente Navarro, "The Underdevelopment of Health or the Health of Underdevelopment: An Analysis of the Distribution of Human Health Resources in Latin America," International Journal of Health Services, 4 (1974), 5 - 27.

set by developed Western countries, but they are inappropriate to the circumstances of low income countries and, hence, are very cost-ineffective. Moreover, the political will necessary for reorienting health care, redistributing services, and training health personnel for practical, population-based, and assertive service is typically lacking. In this way, elitist health systems having little popular impact are perpetuated.[30]

That, at any rate, is the stereotype. Both the stereotype and the performance gap conveyed by it suggest a number of openings for useful research. Studies are needed on the origins of existing health systems in low income countries; on their structure, priorities, and resource allocation (spatially and functionally); on their personnel recruitment, training, and deployment; on their identification of and response to problems; and on their knowledge of health needs in the society, their modus operandi and performance. It is important to learn how different systems reconcile modern with traditional medicine, how and for what purposes doctors are trained, to what extent and how paramedicals are incorporated into modern health delivery, what blends of preventive and curative services exist, how different components and combinations of "integrated delivery" of nutrition-health-family planning services have been put together, where initiative for health care lies -- with the public or with the system itself, whether and how outreach is achieved,

[30] See, for example, Nancy Birdsall, "Health Planning and Population Policy in Africa," African Studies Review, 19 (April 1976), 19 - 33; and Ichak Adizes and Paul Zukin, "A Management Approach to Health Planning in Developing Countries," Health Care Management Review, 2 (Winter 1977), 19 - 28.

what records are kept and how they are used, and -- most critically -- what impact on basic health problems is being achieved.[31]

All of this suggests the need for a practically grounded nutritional review of the health sector. While research on nutrition and disease will continue to inform what health care delivery should do to alleviate malnutrition, more broad-gauged analyses of actual systems in operation will help to define what they are capable of doing in fact, given the assets and constraints that apply in each case. If at a general level it is useful to establish, quite precisely, what reasonable expectations are concerning the role that health infrastructures can play in meeting malnutrition, granted that malnutrition is more than a health problem as such, it is also appropriate to define how they can best play that role and then see what might be done in specific settings.

Conclusion

It is hoped that the three research foci discussed in this paper represent a fruitful way of outlining an agenda for the further study of nutrition, malnutrition, and health. Some of what is broached here may seem, at first glance, to have little to do with nutrient intake and disease response. On the other hand, if the topic is perceived broadly, even the items identified under Research Focus #3 are relevant. Moreover, it then becomes clear that many disciplines come into play and

[31] Model analyses include Oscar Gish, Planning the Health Sector: The Tanzanian Experience (London: Croom Helm, 1975), and Peter Hakim and Giorgio Solimano, Development, Reform, and Malnutrition in Chile (Cambridge: MIT Press, 1978).

that at least a modicum of interaction among them is desirable Specialists working in the different concentric circles will have to share knowledge and insight with one another at the same time that they pursue their individual lines of inquiry. The challenge for research is to combine cross-fertilization with specialization. This is the key to developing new knowledge that is not only intellectually exciting but useful in the practical, policy sense as well.

ENERGY INTAKE AND FUNCTIONAL COMPETENCE
COGNITION AND SENSORY ACTIVITIES: BIOLOGICAL ASPECTS*

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Presented at the US AID Workshop, Washington, D.C., 2-6 October 1978

Preamble

Behavior, including the cognitive aspects, is a complex resultant of the interaction between organisms and their environments, physico-chemical and sociocultural.

In this communication we shall address ourselves to five topics:

(1) Nutrient intake and nutritional status

(2) Behavioral and organismic criteria of function

(3) Beyond sensory thresholds

(4) Are adults immune to malnutrition?

(5) The role of biological (nutritional) and social factors in malnutrition

Literature on "malnutrition and brain development" was summarized by Myron Winick (1976) and will not be reviewed here, even though it deals with an important aspect of the biological bases of behavior and of potential impairment of behavior by severe malnutrition experienced in early infancy.

While the point has not been made explicitly in the communications we have received, I believe I am correct in assuming that the project is to involve a study (or studies) on man, not on subhuman species. For this reason alone I have not dealt with the extensive animal literature.

In the context of the present discussions, nutrient intake means "energy intake" (or at least primarily energy intake). Such an emphasis is justified, both in terms of the needs of the developing nations and as a counterbalance to recent overemphasis on protein deficits. This should not be interpreted as disregard for the role of protein in the diet. While energy ("food") deficits will be of central importance in the research that we are to consider, we cannot lose sight of the behavioral significance of nutritional deficiencies involving minerals and vitamins (especially iron, iodine, and vitamin A) and their frequent co-existence with energy deficits.

I have encountered several kinds of problems in preparing this report and in attempting to relate the activities of this workshop to the project as a whole.

For one, I have the uncomfortable feeling that our model of the behavioral aspects of "functional competence" is Comtean, bipartite,

reductionist. Comte (a mid-19th-century French thinker) negated the right of psychology to existence: in August Comte's view, what we call "psychological" is, in reality, either the subject of biology or of sociology. In this perspective, the two "state of the art" reports are to deal with the biological and the social aspects of cognition.

I favor a tricomponental, tripartite model. The three components or aspects are the intraorganismic processes, individual behavior, and interpersonal (social and, more broadly, environmental) interactions. Clearly these are all aspects of the activities of organisms-in-the-environment. Only for purposes of analysis does it make sense to consider them separately. Cognition is a class of behavior of individual organisms. My point is that in the scheme of job assignments this critical, central, "psychological" component is missing.

The focus of research that we are to consider is on the relationship between nutrient intake and the ability to function in society. In a vague sort of way, this has been the concern of all research on malnutrition and behavior. In reality, we have limited ourselves -- with exceedingly rare exceptions -- to the criteria of statistical significance.

I found it useful to think in terms of what I call the "biological" significance of a change resulting from a deficient diet. The biological significance may be assessed by relating the magnitude of the change (Δ) to the variability of a given measure under control conditions. Thus an "index of biological significance" of a change may be computed as:

$$I_{BS} = \frac{\Delta}{SD_C},$$

where the SD_C refers to the standard deviation of the values of test scores for a given variable during the pre-experimental, control period.

Let us consider in this framework the data on changes observed in a variety of psychomotor functions after 6 months of severe food restriction (Keys et al., 1950, p.705).

Statistically, all the changes were highly significant. The index of "biological significance" helps us to separate the test into two groups: the tests of strength that were markedly affected, reflecting the loss of muscle mass, and the various tests of speed of movements

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Table 1. Biological significance of changes in motor functions. C = control data, S24 = mean scores in the 24th week of severe food restriction, Δ = [C-S24], SD_C = standard deviation of the test scores at the end of the control period

Test	C	S24	Δ	$\frac{100\Delta}{SDC}$
Hand dynamometer, kg.	58.2	41.8	-16.4	2.2
Back dynamometer, kg.	165.4	116.1	-49.3	1.8
Gross body RT, in 1/100 sec.	42.3	45.6	+3.3	0.9
Speed of arm movements, no./min.	75.3	71.4	-3.9	0.7
Tapping speed, taps per lo sec.	66.6	63.2	-3.4	0.6

Table 2. Estimated general magnitude of semi-starvation effects resulting from different average losses of body weight in adult populations (derived from a variety of sources).

Percentage of Body Weight Lost	Magnitude of Semi-Starvation Effects		
	Civil Disorder and Strife	Capacity for Prolonged Physical Work (%)	Actual Work Performance (%)
5.....	Slight	(?)	-10
10.....	Moderate	-10	-20
15.....	Serious	-30	-50
20.....	Very serious	-50	-80
30.....	Moderate	-80	-90
40.....	Slight	-95	-95
50.....	None	None	None

for which the effects were substantially less severe.

Beyond the biological significance lays the murky realm of "practical" (or social) significance. We have climbed on this very fragile limb when we asked (Keys et al., 1950, p.917): What is the probable relationship between the magnitude of weight loss resulting from deficient food intake and 3 socially relevant "outcome" variables: civil disorder and strife, capacity for prolonged physical work, and the probable actual performance of physical work. Our best guestimates are indicated in Table 2.

While going beyond the "safe" tests of statistical significance means skating on thin ice, we cannot escape, for ever, the legitimate questions "What does it all mean?", asked by the planner and, more and more, by administrators of research funds. Improved nutrition is a part of public health, and we must give serious attention to the "cost-benefit ratios," uncomfortable, yes, painful as this may be.

1. Nutrient intake and nutritional status

The ultimate goal of the AID project has been defined as the exploration of the relation between nutrient intake and functional competency. The workshop is focused on the cognitive area, including the special senses.

It may be useful to remind ourselves that, for present purposes, "nutrient intake" means primarily the intake of energy, of calories.

We can measure, precisely and dependably, the energy intake in a metabolic ward and, when due precautions are taken, in a physiological laboratory.

In the field we must be satisfied with approximations which are, typically, rather gross. This is a compelling reason why in research on malnutrition and behavior we have related behavior to the outcome of nutrition, i.e., nutritional status, "nutriture." Furthermore, and very importantly, information on energy intake is of very limited value unless we know also, with reasonable precision, the energy output. Man can maintain body weight at remarkably different levels of energy intake. People can become fat on an intake of 2,000 calories

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per day, and lose weight on an intake of 5,000 calories per day. The critical aspect is not the absolute intake but the balance (or the lack of it) between intake and output.

I am not arguing against the need to pay more attention to nutrient intake. I am arguing for the clarification of concepts and improvement of procedures for the assessment of nutriture. The amount of confusion is distressing, even with reference to such basic criteria of nutritional status as "stunting" and wasting," applicable to children living under conditions of chronically deficient or at most marginal nutrient intake: "stunting" refers to retardation (deficit) in height for age, while "wasting" indicates that the child's weight is too low for its height.

The techniques vary over a wide range along the simplicity-complexity dimension, from a "QUAC stick" to assessment of nutriture in terms of a sophisticated analysis of body composition (Brožek 1974).

In the area of clinical malnutrition of the young child, a novel approach to the synthesis of biochemical and clinical data obtained at the time of hospitalization for energy - protein malnutrition was used in a study carried out in East Africa (Hoorweg 1976, p.49).

On admission the condition of the children, 8 to 27 months of age, was characterized in terms of 7 variables. Their factor analysis yielded two principal components which I prefer to call a "K" component ("K" standing for "kwashiorkor") and an "M" component ("M" for "nutritional marasmus"). The "K" component (or dimension) of clinical energy-protein malnutrition is characterized by the presence of edema and skin changes, high overall ratings of clinical severity of the patient's condition, low level of serum protein, large weight loss after admission (reflecting primarily the loss of water), and small difference between actual body weight and body weight expected for age. By contrast, the dominant feature of the "M" factor is dramatic wasting (reflected in very low body weight) and low hemoglobin level. Skin changes are absent, as is edema. The serum protein is not markedly depressed. The author, J.C. Hoorweg, has chosen -- unfortunately, in my opinion -- to call these 2 components "acute malnutrition" and "chronic malnutrition."

For each child the magnitude of these two components, indicating the severity of the kwashiorkor-like and marasmus-like aspects of

"nutritional status," is computed as a weighted index, using the values of the original seven variables and the weights given in Table 3 (from Hoorweg 1976, p.49):

Table 3. Medical indicators at admission: varimax rotation of first two principal components (mal- malnourished groups pooled; N = 3 x 20).

	dimension 1	dimension 2
percentage of expected weight for age[a,b]	.07	-.80
percentage of weight lost after admission	.58	-.55
haemoglobin level[b]	-.28	-.66
serum protein level	-.59	-.10
oedema	.73	-.17
skin changes	.69	.00
overall clinical severity[c]	.73	.23

(a) Baganda standards (Dean, 1954; Rutishauser, 1965).
(b) lowest level during hospitalization.
(c) as judged by the attending doctor.

The scores computed for each of the two components were then used as a point of reference for the analysis of the behavioral data obtained in these children some 12 years later.

It came as a surprise -- at least to me -- that the correlations between the children's "K" scores and 9 psychological tests administered to the children in their teens were low, statistically not significant, and random in direction: four indicated a negative, and five a positive relationship.

By contrast, the "M" scores correlated negatively with test scores obtained later in life: the greater the "M" scores, the lower the subsequent performance on Raven matrices, block design test, memory for designs, and arithmetic (Hoorweg 1976, p.75). Children with high "M" scores in infancy tended to be somewhat less energetic and more docile in their teens.

2. Behavioral and Organismic Criteria of Function

The behavioral methods used in the comprehensive Minnesota study on the effects of severe energy deficits, imposed on young adult male volunteers over a period of 6 months and resulting in the loss of one-fourth of the pre-experimental body weight, described in detail elsewhere (Keys et al. 1950, pp.1094-1104), may be grouped into 4 categories:

I. Special senses: Auditory acuity, visual acuity, flicker fusion frequency, perceptual fluctuation (reversals of perspective in which a geometric cube design was seen).

II. Motor functions: Strength, speed of movements (tapping, hand plus forearm movements, gross body reaction time, speed of leg movements), and coordination of movements.

III. Intelligence: The Institute of Educational Research (Columbia University) CAVD Scale (Completions, Arithmetics, Vocabulary, Directions), test battery based on Thurstone's factorial studies of intelligence, and test of learning ability ("Crossing out 4's; 18 successive 1-min. trials per test session).

IV. Personality: Interviews, diaries, Minnesota Multiphasic Personality Inventory, Guilford's Inventory of Temperamental Traits, self-ratings, complaint questionnaire, man-by-man ratings, drive ratings.

Standard methods used in research on malnutrition in children, frequently with local modification, have been described (Klein and Adinolfi 1975; Hurwitz 1976) and will not be listed here.

Additional tests and measuring techniques have been devised ad hoc, e.g., a technique for the characterization of the activity level of the very young child (Chávez, Martínez, and Bourges 1972). A number of the procedures are "biological" in nature or have a biological component. Among these methods, applied in the context of research on malnutrition, are procedures for the study of the habituation of the orienting response in terms of the magnitude of deceleration of the heart rate (Lester 1975), the characteristics of cry sounds (Lester 1976), level of arousal and latency or response to an auditory stimulus (Griesel 1972), as well as the electrical activity of the brain and speed of nerve conduction (Coursin 1974, Rhodes and Snyder 1975, Taori and Pereira 1974).

3. Beyond Sensory Thresholds

We have noted (Keys et al. 1950, p.675) that the special senses provide information about the environment and that their adequate functioning is essential for effective interaction between the organism and the changing environment. Consequently, receptivity to sensory stimuli is an important aspect of cognitive function -- taking the term in a broad sense. In addition, some of the sensory functions provide a valuable physiological avenue to the functional status of the central nervous system (cf. Beck and Dustman 1975, esp. pp.205-206, Callaway 1975).

Following the Second World War, dimness of vision (amblyopia), deterioration of visual acuity, and narrowing of the visual field were frequently reported in Allied prisoners of war and civilians interned in the Far East (Keys et al. 1950, pp. 676-679). Occasionally, nerve deafness was noted. It is very probable that in these situations severe vitamin deficiencies (and perhaps the presence of toxic factors) were superimposed on energy deficits. Such an hypothesis is supported by field reports from areas of Europe in which severe food deficits were present. These reports contained little reference to disturbances of special senses, except for night blindness -- a peripheral rather than a central phenomenon -- due to the changes in the light sensitivity of the receptors (Keys et al. 1950, pp.675-676).

The hypothesis that visual disturbances observed in the Far East were due to factors other than deficits of calories is further strengthened by the fact that in an experimental study of the effects of severe food deficits (Keys et al. 1950, pp.684-658) the changes in visual functions were either absent or negligible. Visual acuity, measured at two levels of illumination at the plane of the test patch (1 and 100-foot candles respectively), remained unaffected by the loss of one-fourth of body weight. Similarly, perceptual fluctuation did not change. The frequency at which successive light flashes appear to fuse into an uninterrupted light served as the indicator of the resolving power of the retino-cortical system. In the Minnesota study there was a very small but consistent (and, consequently statistically significant) decrement of the fusion rate.

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No deterioration was observed in the acuity of hearing. In fact, the measured acuity improved during the period of food restriction. Reports of the subjects (who were not aware of their audiometric scores) were consistent with the audiometric findings. A number of the men reported that their tolerance for loud music, speech, and noise was lowered. The observed decrease in auditory thresholds (indicating increased acuity) could be interpreted as a random effect or as a result of instrumental artifact, were it not for the fact that the trend was reversed during the period of nutritional rehabilitation. After 12 weeks of controlled refeeding the level of auditory acuity returned to the pre-experimental, control values.

In research on the effects of energy and protein deficits we have to go beyond the study of sensory thresholds and examine more "cognitive," perceptual (rather than sensory) functions. One of the processes that has attracted the interest of investigators of the behavioral effects of generalized malnutrition is "intersensory intergration." The technique for the study of "intersensory development" was developed by Birch and Lefford (1963). Under the label of "neuro-interactive functioning," the phenomena of cross-modal matching of patterns (auditory-visual, visual-kinesthetic, haptic-kinesthetic, visual-haptic, kinesthetic-visual) are considered at length, in nutritional context, by Cravioto and DeLicardie (1975, pp.46-70).

The approach was covered, in the section on "specific function tests," in Hurwitz's review (1976, esp. pp.95-96) of tests used in research on the behavioral effects of malnutrition. Hurwitz notes that findings, reported in the literature and indicating that children with a documented history of clinical energy-protein malnutrition during infancy perform less well on intersensory tasks than controls, may reflect differences in the mastery of language and need to be interpreted as being conceptual rather than perceptual in nature.

Recent data on the effects of clinical energy-protein malnutrition in infancy on cross-modal matching were reported by Srikantia (1979, in press). The differences between the index children and the controls (Table 4) in visual-kinesthetic, visual-haptic, and haptic-kinesthetic comparisons are statistically highly significant at the age 8-9 years but decrease markedly during the next 5 years. At the age of 15-16 years the test no longer possesses discriminatory capacity since at

Table 4. Mean differences between the error scores of the index children (N = 19) and the control children (N = 19) on tests of intersensory integration. SE = standard errors of the means; t = tests of statistical significance of the mean differences, associated with 36 degrees of freedom ($t_{0.05} = 2.03$, $t_{0.01} = 2.73$, $t_{0.001} = 3.60$).

Age (years)		COMPARISONS					
		Visual-kinesthetic		Visual-haptic		Haptic-kinesthetic	
		Equivalence	Non-Equivalence	Equivalence	Non-Equivalence	Equivalence	Non-Equivalence
8 - 9	M	7.2	3.1	5.3	1.4	9.1	3.4
	SE	2.35	0.85	0.96	0.34	2.2	0.90
	t	3.06	3.65	5.52	4.12	4.14	3.78
13-14	M	0.6	0.5	1.0	0.5	1.2	1.45
	SE	0.38	0.28	0.32	0.31	0.64	0.74
	t	1.58	1.78	3.12	1.61	1.88	1.96
15-16		At this age none of the children in either group made any errors					

this age the performance of all children was error-free. The test, at least the form that has been used, is "age-specific," i.e. is applicable only to younger children.

The Bender Gestalt Test (Bender 1938, Koppitz 1964, Tolor and Schulberg, 1963) is classified by Hurwitz (1976, p.96) as a paper-and-pencil visual (perceptual) motor test, involving the copying of geometrical figures.

Green (1979) used the test effectively in studying the behavioral correlates of iodine malnutrition. The severely affected individuals (deaf-mute cretins) had dramatically higher error scores than the "normal" adults of the community (see Table 5).

Table 5. Mean number of errors on the Bender-Gestalt Test

	Deaf-Mute Cretins		"Normal" Adults	
	Males	Females	Males	Females
$\bar{X}$	9.8	15.9	1.8	3.8
SD	5.7	4.6	2.1	2.9
N	25	20	111	165

4. Are adults immune to malnutrition?

One of the considerations I sorely miss in the preliminary discussions of "the research project" that the workshops, jointly, are to help to design is the consideration of <u>age</u>. Age of the potential subjects has far-reaching, many-sided implications. The majority of behavioral methods is age-specific. The age of applicability of a test is frequently quite narrow, and one of the problems in the study of young children is that we have to <u>change</u> the tools as children increase in age.

Age of the subjects has important ethical implications: On

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ethical grounds, no dietary deficits can be imposed on children, and any "experimental" manipulation of the diet has to be limited to the kinds and amounts of supplements -- and even then there are problems, a plethora of them. The cessation of supplementation, in field studies, is one of the thorniest.

On the positive side, longitudinal studies in children make it possible to use rates of physical growth and mental development as a valuable dependent variable.

One of the unresolved issues is the long-term significance (if any) of the age at which infant malnutrition occurs, i.e., operationally, of the age at which the child is admitted to the hospital.

But, in connection with the considerations of age, the single most important, greatly overlooked issue is the significance of malnutrition (primarily caloric undernutrition) in the adults. The perusal of the literature clearly indicates that in the last 20 years or so the human studies on the effects of energy and protein deficits have been heavily concentrated on the young child. This is fully understandable since this age group is particularly vulnerable to deficits of energy-yielding food stuffs and of protein. It is at this age that the severe, clinical forms of energy-protein malnutrition -- kwashiorkor, nutritional marasmus, and marasmic kwashiorkor -- occur.

Investigations of the effects of undernutrition in school children are few and, typically, represent follow-up studies of children who experienced clinical malnutrition early in life.

Experimental investigations on the behavioral effects of calories and vitamins in adults were stimulated by the needs of the Second World War and, to a lesser degree, the Korean conflict. This type of research all but disappeared in the last 2 decates, and most of the studies on adult man that have been reported are concerned with the physical aspects of work capacity in iron-deficiency anemia (Viteri and Torún 1974, WHO 1975), with emphasis on cardiovascular functions and energy cost of work.

Adults are breadwinners. They are fathers and mothers, and their interaction with the infants and children is a critical factor in the child's mental development.

A widely-spread myth seems to have developed that malnutrition affects only the behavior of children. As is typically the case, there is a grain of truth in this myth: Except under conditions of famine, in adults we rarely see extreme wasting and/or excessive body hydration manifested in edema. Kwashiorkor, nutritional marasmus, and a syndrome combining the features of the two is typically seen in early childhood. So far so good. But is is woefully misleading to state, as has been done in print recently (Manocha 1975, p.403) that "there is no evidence that the adult population suffers from any mental impairment under the influence of malnutrition."

While in severe undernutrition (Keys et al. 1950) the most dramatic decrement was observed in endurance in tasks requiring a large though brief output of energy, there was also a marked decrease in strength as well as in the level of self-initiated activities. The latter phenomenon reflected a profound change in motivation, not in capacity.

In research involving performance we cannot disregard the simple-looking equation:

$$P = C \times M,$$

i.e., performance involves both capacity (C) and motivation (M) This is a symbolic equation, nota mathematical formula. Yet it is of fundamental importance, whether we deal with physical work or with cognitive, intellective activities.

In our study on the behavioral effects of severe undernutrition (Keys et al. 1950), in investigating the area of cognitive (or, more precisely, intellective) functions, we utilized all the major tools then available and added some "home-made" ones for better measure. We used tests ranging from a minute in duration to a test for the completion of which the subjects took between 8 and 10 hours, divided into several (usually 3) sessions. We have examined the effects on the subjects' "mental level" (using "power tests," i.e. tests without predetermined, strict limits) and speed tests, short in duration and with rigorous time limits. We measured "learning ability" by following improvements in the performance on a short test (Crossing out 4's) repeated 18 times during a test session, with 90 seconds between the separate trials.

What did we find? As time went on, during the "experimental" (restriction) phase of the study, complaints of inability to concentrate for any period of time and of difficulty in developing coherent thoughts became numerous. Toward the end of the 6-month period of severe energy deficit a large proportion of men felt that their judgment had been impaired. They reported that their general alertness and comprehension declined.

By contrast, measured intelligence did not change importantly during either the period of food restriction or the subsequent period of nutritional rehabilitation.

At the same time, let me repeat, spontaneous mental effort and achievement (such as writing letters) declined markedly during food restriction, remained at a low level during the early phase (the first 12 weeks) of rehabilitation, and only gradually returned to "normal."

It was the narrowing of interests (heavily centered on food), apathy, and lack of initiative in carrying on conversation or other kinds of intellective activity which led the men to feel that they had suffered actual loss of intellective power. Importantly, the study program initiated by the group itself and designed to train the men for reconstruction service in Europe failed to hold their interest and had to be discontinued.

Did this study, unique -- in many aspects -- in the annals of nutritional research, answer <u>all</u> the questions about the effects of energy deficits? It did not and could not. The study had built into it a desideration of a loss of one-fourth of initial, pre-restriction body weight in a group of "normal-weight" individuals. The weight loss proceeded at a predetermined, decelerating rate, with the weight-loss curve reaching a zero slope toward the end of the 6th month. Different <u>rate</u> of weight loss would almost certainly affect the functional changes.

While 6 months felt like eternity, both for the subjects and for the experimenter, it is a period close to semi-starvation experienced during war-time, and this is what we wanted to "model." But what happens under conditions of chronic and -- to make matters more complex yet -- multi-generational food deficits? We have seen a multiplicity of "adaptive" changes taking place during six months, including decline in basal metabolism. This response was prompt and steady.

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This is a favorable, "adjustive" change since it reduces the net calorie deficit, i.e., the deficit compared with the enery deficit which would have prevailed in the absence of a reduction in the basal metabolism. To an individual on a severely restricted food intake the reduction of basal metabolism means that, at a given food intake and energy output, not only his rate of weight loss but also his rate of the loss of strength and endurance is diminished and that, if the condition persists, he will live longer. In the Minnesota study, at the end of the 6th month of the deficiency, the total rate of basal metabolism was almost 40% less than in the control period. It was calculated that this represents the saving of almost 600 calories per day.

Other indicators of the general slowing down of the machinery of the body included the decrease of basal pulse rate from 56 to 43 beats/minute and the decrease of systolic blood pressure from 105 to 97 mm. Hg.

It should be noted that the weight loss curve reached a zero slope at the 24th week of food restriction, even though the average daily energy intake (1642 calories) was very close to the initial intake of 1658 calories, compared to the 3500 calories required for the maintenance of steady body weight during the control period. The subjects were able to maintain a steady body weight on less than one-half of the energy input.

How was this achieved? What were the mechanisms of the adaptation? We have discussed one of the factors: the reduction of basal metabolic rate. A small reduction in calorie expenditure is due to reduced food intake; we calculated specific dynamic action (S.D.A.) of the ingested food as 7.5% of the caloric intake. By far the largest contributor was reduction in physical activity. The data are given in Table 6.

The decrements, as percentages of the control (pre-restriction) values, were as follows: Energy intake (and S.D.A.) decreased by 53%; the calorie equivalent of basic metabolism, by 39%; physical activity, calculated by difference [Energy intake maintaining a steady body weight - (S.D.A. + B.M.)], decreased by 66%. For comparison, body weight decreased by 24.2%.

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Table 6. Breakdown of calorie expenditure in the Minnesota Experiment

	Control	S24	Δ	Δ%
(1) Energy intake	3492	1642	1850	53
(2) S.D.A.	262	123	(139)	(53)
(3) B.M.	1576	961	615	39
(1)-(2+3) Physical Activity	1654	558	1096	66
Body weight, kg.	69.4	52.6	16.8	24.2

This is the best physiological estimate of the overall decrement in physical (muscular) activity of initially normal young men over a period of 6 months of severe restriction of food intake. It is the single, most comprehensive "biological" (metabolic) indicator of the profound changes in gross motor behavior that take place in "chronic" situations calling for the conservation of energy expenditure: In popular language we would be tempted to call a severely, chronically malnourished individual "lazy." In first encountering the working population in under-developed countries, maintaining a precarious balance between energy input and output, such a temptation is almost irresistible.

5. The role of biological (nutritional) and social factors in malnutrition

In the early studies on the behavioral aspects of malnutrition, the underlying model was simplicity itself: N → B. In time the model became much more complex by the addition of other factors and the incorporation of feedback loops.

The most important added factor was the impact of the socio-economic environment. I fully agree with Jack Tizard (1974) and others that the impact of malnutrition on behavior is an "ecological" problem. I have been impressed by Herbert G Birch's moving comment (1972, p.781): "Malnutrition never occurs alone, it occurs in conjunction

with low income, poor housing, family disorganization, and climate of apathy, ignorance and despair." But we must avoid two pits into which it is all too easy to fall:

1) We can readily forget that Birch is talking about malnutrition as it occurs in the field.

2) We must avoid the temptation to elevate the complex of the " SES " (socio-economic status) variables into the driver's seat and essentially disregard the nutritional input and metabolic mechanisms.

To tease out the single etiological strands from an interlocking etiological fabric is by no means simple but we cannot give up too readily if we wish to understand the phenomena with which we are to deal on a practical level.

I shall note two recent efforts to unscramble the nutritional and the social components within the socio-economic matrix of poverty.

The first effort was directed to the study of "experiments in nature," i.e. of illness resulting in severely impaired nutrition in children, in industrially developed countries and in families in which access to food was not limited by financial considerations. I am referring to studies on the behavioral sequelae of infant malnutrition associated with neonatal resection of the ileum (Valman 1974), pyloric stenosis (Berglund and Rabo 1973; Klein, Forbes and Nader 1975) and cystic fibrosis (Ellis and Hill 1975; Lloyd-Still et al. 1975)

The second effort at the assessment of biological (nutritional) and social factors may be illustrated by two different approaches.

The first of these deals with the sequelae of energy-protein malnutrition requiring hospitalization. The subjects were Jamaican boys hospitalized, with a primary diagnosis of malnutrition, at the ages of 6 to 24 months. Taken as a whole (Richardson 1975), at school age these children were significantly smaller in height (but not in weight) and head circumference than their unrelated classmates and neighbors matched for age and sex, had a lower intelligence, and did significantly less well in school. They were rated by their parents more often as backward, withdrawn, and unsociable. At the same time, consideration of the characteristics of the social environment of these children (specifically, the caretaker's level of capacity, the quality of home furnishings and appliances, and intellectual

stimulation) indicated that the children who had suffered from malnutrition in early childhood came from more disadvantaged backgrounds than the peer controls.

But the really interesting and new facts emerge when one segregates the index cases in reference to the 2 sets of factors: nutritional (using height at follow-up at the age of 6 to 10 years as an index of chronic inadequacy of nutrition) and social background history (Richardson 1976).

For children who are tall and whose social background is favorable, the mean I.Q. of the index and the comparison children are almost identical (69 vs. 71).

For children of shorter stature (regarded as indicative of chronically poorer nutrition) but whose social background is favorable the differences are still small (62 vs.65), although the level is lower.

For children who are tall ("better nourished") but whose social background is unfavorable the differences are more marked and the level still lower (55 vs. 62).

The combination of low stature (chronically poorer nutrition) and unfavorable social background yield, as one might expect, the lowest level and the largest differences between the index and the control children (49 vs. 58).

While the sizes of the four subgroups are small and the findings call for confirmation, the results are compatible with a model according to which an episode of clinical malnutrition in infancy has different consequences for intellective function depending on: 1) nutrition (and, one should add, health) in the years following recovery from clinical malnutrition, and 2) social background.

The two -- or more precisely 3 -- sets of factors are synergistic: severe malnutrition during infancy, and nutrition and social environment during childhood.

The second set of data refers to a longitudinal study (Brozek, Coursin and Read 1977) carried out at Guatemala (Irwin et al., in press). This study was carried out at four isolated Ladino (Spanish speaking) villages of rural Guatemala where moderate energy-protein malnutrition is endemic. The residents of the villages, matched on

a number of demographic, social and economic characteristics, are engaged in subsistence farming. The median family income corresponded to about $200/year. The average family size was 6.5 members.

The mothers and young children of 2 of the 4 villages were offered a beverage referred to as "Atolé," containing about 160 calories and 11 grams of protein per cup. Two other villages received "Fresco," a beverage substantially lower in calories (60 calories per cup) and no protein. Both beverages contained vitamins and minerals. Apparently the supplementary beverages had very little effect upon customary home consumption.

The supplements were provided to mothers starting early in pregnancy -- as soon as they chose to come to the distribution centers. Children were given supplements as soon as the mothers brought them to the centers, usually around 9 months of age or later.

The cognitive aspects of mental function were assessed by several test batteries, appropriate for children of different age levels: neonates, infants, and preschool children.

In the Guatemala study the independent (nutritional, interventional) variable was the amount of supplemtary calories ingested by the mother during pregnancy and lactation, and by the child up to the point of test administration. The amount of individual supplementary nutrient intake, correlated positively with prenatal and postnatal physical growth. What effects, if any, did it have on mental development? Furthermore, what was the relative contribution of the supplementary intake of calories and of the quality of the home envornment? The latter is the critical question for the present purposes.

Mental development was measured by two batteries of tests: 10 tests were administered at ages 3 and 4, and 22 at the ages of 5, 6, and 7 years. The tests were chosen to tap a variety of intellective abilities including reasoning, learning, and memory, as well as perceptual analysis. The test, constituting the "Preschool Battery," were adapted to the local setting by a team of North American and Guatemalan psychologists and a Guatemalan cultural anthropologist.

The index of the quality of home environment is based on variables related to 1) nutrition (home diet, diarrhea), 2) the economic situation of the family (characteristics of the family dwelling -- its

size, number of rooms, and type of construction; type of clothes worn by the parents), and 3) the personal-social characteristics of the child's micro-environment: Mother's vocabulary score, years of schooling, literacy level, and "modernity"; the amount of time the father spends with the children; provision of toys by the parents; attempts to teach children at home; and the presence of decorations on walls and availability of printed matter in the house. This third group of variables is an indicator of the amount of intellectual stimulation available to the child at home.

We shall limit ourselves to a single issue: What are the percentages of the variance of the composite test scores accounted for by the Quality of Home Environment (QHE) and by the amount of supplementary calories ingested by the mother during pregnancy and lactation and by the child up to the point of the administration of mental tests?

Table 7. Percentage of variance in Composite Test Scores accounted for by 1) Quality of Home Environment (QHE), considered alone, and 2) the supplementation calories (SC), with the effects of QHE first removed. The degrees of freedom vary for boys and girls, and for different ages.

Factor	Age, in years				
	3	4	5	6	7
BOYS					
1) QHE	4.9+	7.6**	21.6**	14.0**	13.7**
2) SC	6.0**	4.2**	5.4*	5.2*	4.2+
GIRLS					
1) QHE	6.9*	6.5*	9.8*	14.8**	22.6**
2) SC	5.2*	2.1	3.6	2.7	4.2

p values: + < 0.10
* < 0.05
** < 0.01

The Quality of the Home Environment makes a substantial contribution to the Composite Score variance (Table 7). The contribution tends to increase with the age at testing. This tendency is particulary marked in the girls.

After controlling for the effects of QHE, supplementary calories still make an important contribution to the test scores, more so in boys than in the girls.

The authors (Irwin, Klein, et al. 1979, in press) referring to the presence of a small but not negligible contribution of supplementary calories to the variance of the Composite Scores, stress that "This is a particularly important point, since many early studies of the relationship of nutritional status to mental development have not been designed so that one could decide whether the quality of the home environment was not in fact responsible for observed associations between malnutrition and poor mental-test performance."

Full results of a complex, stepwise regression analysis, including the effects of treatments (Atolé vs. Fresco) and interactions, will be reported in the authors' published account.

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SITE VISIT, INDONESIA
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D.H. Calloway

I. Indonesian Nutrition Research and Development Center - Bogor, Indonesia

A. Organization and Administration

The Center is administratively located in the Ministry of Health. The Director is an Indonesia-trained M.D., Ph.D., Darwin Karyadi; his English competency is quite good, spoken with a Dutch-Indonesian accent. There is no assistant director.

The professional staff numbers about 16 (at least one is presently on study leave, working toward a graduate degree) although the nominal complement is 25. Three, including the Director, hold the Ph.D. degree. There are several technicians, trained to the B.S. level.

The Center is organized in four divisions, each with four sub-divisions as follows:

A. Community Nutrition (Miss S. Martoatmodjo, M.P.H.)
   1. Epidemiology and Surveillance
   2. Clinical Nutrition
   3. Communication
   4. Growth and Development
B. Nutritional Biochemistry (Mr. Muhilal, Ph.D., U.S.-trained biochemist)
   1. Nutritional Requirements
   2. Hematology
   3. Metabolic Studies
   4. Animal Experimentation
C. Food Science (Mr. Hermana, doctoral student in U.S.)
   1. Food Chemistry
   2. Food Microbiology
   3. Food Toxicology
   4. Food Preparation and Testing
D. Socioeconomics and Statistics (Mr. Djumadias Abunain, M.S., Nutrition)
   1. Program Analysis
   2. Consumption Studies and Agroeconomics
   3. Social, Cultural and Economic Studies
   4. Data Processing and Statistics

I was unable to identify any staff members fully qualified to carry out research on nutrient requirements or metabolic studies and I gather no such work has been done, although it is planned.

B. Facilities and Resources

The Center consists of two main buildings: a one-story structure containing offices, library, food preparation and testing room, and statistical laboratory; and a two-story structure where the chemistry and microbiology laboratories are located. Some of the instrument rooms are individually air-conditioned. The Director lives in an adjacent residence.

New buildings are to be completed in the period 1979-1981. The new construction is to include a metabolic unit.

The biochemistry laboratories are now equipped to carry out analyses of biological materials for amino acids, vitamin A, carotene and retinol-binding protein. There is no atomic absorption spectrometer or other equipment that would permit trace element assays. The food science laboratories appear to be equipped for only routine chemical and bacteriological studies, although research on mycotoxins is said to be in progress. The food preparation laboratory is poorly equipped and would not meet U.S. sanitation codes. There is no computer facility in the Center or elsewhere in Bogor; data are processed in Jakarta.

The library is in woeful condition. The holdings are minimal and even the abstracting journals are several years out of date.

IBRD has included this center in its Indonesian project and will provide U.S. $5.9 million over a four-year period for construction, training and support. (See IBRD Report No. 1318-IND.)

C. Assessment

Dr. Karyadi appears to spend nearly full time in his role as administrator and is not directly involved in research except at the program-planning level. His Ph.D. research dealt with some aspects of anemia/work productivity/physical capacity and was carried out in conjunction with the doctoral project of Samir Basta (now IBRD).

The biochemistry operations are clearly the most advanced of Center activities. Dr. Muhilal is well-trained, understands methods and equipment. None of his instruments was "down" and technicians were working even though the senior staff were away, attending a conference.

The present staff could not conduct the research projected for our program, nor would they be able to carry out sophisticated

metabolic studies or extensive surveys. They lack everything but enthusiasm. Dr. Karyadi inquired about training opportunities at Berkeley and I encouraged him to send candidates for advanced training for his projected human research activities. I indicated that the Graduate Division would consider applications for M.S./Ph.D. programs or, alternatively, that we would provide non-degree training on a Limited Status admission basis.

I hope that some of the senior staff will visit functioning metabolic research units in the U.S. before they complete plans for construction and equipment, and I have encouraged them to do so.

II. LIPI Workshop on Food and Nutrition in Indonesia

The Indonesian Academy of Sciences (LIPI) convened a national workshop to consider current food and nutrition problems, as a follow-on from a similar meeting held in 1968. The U.S.-N.A.S. sent a small delegation of scientists to serve as resource people during the workshop.

In his opening address, Professor Vernon Ruttan (University of Minnesota, leader of the U.S. delegation) reviewed changes in the agricultural economic situation from 1968 to 1978. He cited as gains increased productivity and growth of the industrial sector; increased rice production as a result of new technologies and of price policies; and slowed population growth rate. Negative factors were increased imports of wheat and rice; increased numbers of families living in poverty; increased numbers of landless laborers and fewer days of employment available to laborers in agriculture; and increased differential in income distribution, worsened because of increased cost of rice relative to income of the poor. Problems identified by Dr. Ruttan as requiring solution were a) resources to be tapped for continued increase in food production (needed are capacity to provide energy efficiently and for rural people to utilize innovations, a scientific establishment, institutions to transmit knowledge, etc.); b) dependency on rice; c) institutional capacity; and d) limitations of conventional economic planning and analysis.

Attendance at this meeting provided an opportunity to meet most of the senior nutritionists presently active in Indonesia. (Participants are listed in Appendix A.) Of the approximately 175 participants, about 50 indicated a primary interest in nutrition; many of these were in related disciplines and not trained in nutrition. The preponderance of nutritionists are in the health/medical sector.

An exception is Professor Sajogys of the Institute of Rural Sociological Research, Bogor Agricultural University, who has been involved in nutrition, household and community research. It was my impression on speaking to him, and Dr. Benjamin White (ADC, Bogor) confirms, that Dr. Sajogys's work is of good, interdisciplinary quality. He would be a key resource for our work. Dr. White also identified two members of the Faculty of Nutrition, Diponegoro University, Semarang, Central Java--Drs. Satoto and Fatimeh--as being good nutritionists in the agricultural sector. Dr. White suggested our contacting Dr. Gillian Hart, ex-Cornell, now Boston University, for additional information. (Dr. Vernon Ruttan has vetted Dr. White himself.)

Ongoing nutrition research in Indonesia is focussed on surveys/surveillance and some aspects of protein-calorie malnutrition, Vitamin A deficiency and anemia. Iodine-deficiency is the other recognized micronutrient problem. Consideration is being given to fortification schemes and MCH measures as direct nutrition interventions.

Integration of nutrition objectives with planning activities seems not to have been effected, even though it is discussed. There is the usual problem of nutrition activities falling within the Ministry of Health and planning efforts focussing on agricultural development without nutrition input. If the recommendation of the Workshop--that nutritional status of the people should be used as the yardstick of success of development programs--is accepted by the government, some coordinating mechanism must be found or there will be internecine conflict (à la USDA, HEW). The mechanism proposed, a ministerial coordinating committee, is unlikely to be effective for the obvious reasons.

III. Potential for Collaborative Work

Indonesia has a full range of nutrition problems and willing investigators. If the health/agricultural interface problems could be overcome, and if the project could avoid accidental perturbation that potentially would come from the smorgasbord of international and bilateral activities in progress/proposed, and if a strong U.S.-institutional linkage could be forged (top U.S. talent willing to spend time in the country and adequate training provided for Indonesian nationals), Indonesia would be a good site. Food patterns include various proportions of the staples--rice, maize corn, cassava--in different populations; there is a variety of climate/soils/agronomic patterns; and terrible deprivation.

Relevant readings from PRISMA, February 1978: Rohde, J.E., et al "Who dies of what and why" (pp 26-38); and Collier, W.L. "Food problems, unemployment and the green revolution in Java" (pp 38-52). Also see working paper U/1/18 from the LIPI workshop, which deals with energy and protein requirements estimates for Indonesia.

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APPENDIX A

SIDANG KELOMPOK SUB-THEMA 1.

MASALAH KECUKUPAN PANGAN DAN GIZI

NUTRITION SUB-GROUP

DAFTAR PESERTA

Ketua : Julie Sulianti Saroso(♀, M.P.H., M.D.?) PROF.

Sekretaris : Ig. Tarwotjo[a,b]

Pemasaran : 1. Darwin Karyadi (M.D.)[a,b]
2. Sajogyo, Prof.
3. Soeharso

"Resource person" : 1. Doris Calloway
2. James Dinning
3. Sunawang
4. Rachmat Qureshi (F.A.O., Asia region)

Peserta :

1. Djumadias Abunain[a,b]
2. Muh. Arief
3. Subiyakto Atmosiswojo
4. M. Amin Azis
5. John A. Dixon (Econ)
6. Wiratmo Haryoko
7. Sayuti Hasibuan
8. Lukas Hendrata
9. Husaini
10. Melati P. Joenoes
11. Kemarajah
12. Sri Kardjati (♀ M.D.)[c]
13. Muhamad Khumaedi
14. Dradjat Prawiranegara
15. Soemilah Sastroamidjojo ♀[d]
16. Lasam Soeroso
17. Lie Goan Hong
18. S. Malasan (M. D.)
19. I.B. Mantra
20. Sukartijah Martoatmodjo
21. Muhilal (Biochem., Ph.D.)[d]
22. Saadillah Marsjid
23. Burhan Napitupulu
24. Sunspendi Notodihardjo
25. Soeharto Prawirokusumo
26. Uton Muchtar Rafei
27. Brata Ranuh
28. Samsudin
29. A. Djaeni Sediaoetama
30. Bambang Setiadi

*Director of Nutrition, Ministry of Healt

a) Authors of nutritional allowances working paper
b) Authors of nutritional status/survey working paper
c) Authors of nutritional survey, E. Java working paper (with Kusin)

31. Hananto Sigit
32. M.B. Sirait
33. H.H. Sitompul
34. Poorwo Soedarmo
35. Soegito
*36. Soekirman (Ph.D.) b
37. Soepardan Soerjohudojo
38. Suhardjo
39. Suharto
40. Sum Suharto
41. Suhartono
42. Haryono Suyono
43. Arifin Tarrif
44. H.A.A. Talaar
45. Bambang Wikantadi
46. Kartono Wirosuhardjo

* Nutrition Planning Bureau of Social Welfare Housing and Health.

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SIDANG KELOMPOK SUB-TEMA 2,

PERANAN TANAH, AIR, HUTAN DAN TEKNOLOGI PRODUKSI DALAM PENYEDIAAN PANGAN

SOIL, WATER, ETC.

DAFTAR PESERTA

Ketua : Sadikin Sumintawikarta

Sekretaris : Surjatna Effendi S.

Pemrasaran : 1. Guswono Supardi
2. Rusli Hakim

"Resource persons" : 1. Colin McClung
2. Donald C. Taylor

Peserta :
1. Doesono Boedidarmo
2. Zaenuddin Harahap
3. Sri Setyati Harjadi
4. Paransih Isbagio
5. Surahmat Kusumo
6. Anris Makmur
7. Harimurti Martojo
8. Soetedjo Moeljodihardjo
9. Hansani Pokerti
10. M. Qazuini
11. Sjamsoeloed Sadjat
12. Sumardi Sastraknusumah
13. A.M. Satari
14. D.T.H. Sihombing
15. Saroso Sindhoesarojo
16. Suwadi Sindoeredjo*
17. M. Soepraptohardjo
18. Soeyono Soeropati
19. Subijanto
20. I.G.N. Tantra
21. Alio Purnomo Tirtoredjo
22. Gombong Tjitroseopono
23. Triharso
24. Andreas Warkidi
25. Suhardi Wirantmadja
26. Sanino Wirjosuhardjo

*Head, Nutrition Unit, Min. Agriculture

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SIDANG KELOMPOK SUB-THEMA 3,
PENELITIAN BIOLOGI UNTUK MENUNJANG TEKNOLOGI PENGEMBANGAN SUMBER DAYA PERTANIAN (TANAMAN, HEWAN, TANAH).

BIOLOGICAL RES.

DAFTAR PESERTA

Ketua : Sotijati Sastrapradja

Sekretaris : Soenartono Adisoemarto

Penrasaran : 1. Didin S. Sastrapradja
2. O. Koswara
3. Johan Silas

"Resource persons" : 1. James Moomaw (AVRDC, Taiwan)
2. Hugh Popenoe

Peserta : 1. Wanda S. Atmadja
2. Didi Atmadilaga
3. L.A. Gunawan
4. Go Ban Hong
5. Komaruddin Ma'sum
6. Sayuti Murad
7. Jetty Nurhajati
8. Ooy Kam Mio
9. P.M. Pajow
10. Soetjipto Partohardjono
11. Roestansjah
12. Susono Saono
13. Muchtar Effendi Sirogar
14. B.H. Siwi
15. Justina Sri Adiningsih Soejitno
16. Aprilani Soegiarto
17. Roberto Soenarjo
18. Martono Soeronegoro
19. Hendro Sunarjono
20. Suryo
21. Sri Suwasti Susanto
22. Mohammad Hasrool Thajib
23. Moses Tjolihur'a

Best Available Document

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SIDANG KELOMPOK SUB-THEMA 4

: KEBIJAKSANAAN PERTANIAN
PERANGSANG BERPRODUKSI

DAFTAR PESERTA

Ketua : Sjarifuddin Baharsjah

Sekretaris: R. Sinaga

Pemasaran : 1. I. Gusti Bagus Teken
2. Affendi Anwar

"Resource Persons" : 1. M.L. Barnett (Anthro, econ, Cornell)
2. Richard Goldman (Econ. new Pakistan)
3. Altaf M. Hussain ?
4. V. Ruttan (Econ; Minn.)

Peserta : 1. Nadir Abdulkadir
2. Anwar Abidin
3. E. Rukasah Adiratma
4. Saleh Afiff
5. Sri Suwito Idris Atmodjo
6. A.T. Birowo
7. William L. Collier
8. Soehartojo Hardjopranyoto
9. Hersojo
10. Erfansjah Hasan
12. Ibrahim Hasan
13. D. Hedley
14. Moh. Mahfoedi
15. Montgomery
16. Mubyarto
17. B.S. Muljono
18. Hidayat Natasatmadja
19. Andung A. Nitimihardja
20. Nyberg
21. Dibyo Prabowo
22. A.M. Saefuddin
23. M. Arifin Selateng
24. Sapuan
25. Kabul Santoso
26. Soekartawi
27. Rusman Sudjana
28. Wahjudi Sugijanto
29. Baskoro Winarno.

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SIDANG KELOMPOK SUB-THEMA 5

TEKNOLOGI LEPAS-PANEN, PENGOLAHAN, PEMASARAN DAN PEMANFAATAN PANGAN

DAFTAR PESERTA

Ketua : Pormadi

Sekretaris : Hermana

Pemasaran : 1. Soewarno T. Soekarto
2. Muhammadi Siswo Soedarmo

"Resource persons" : 1. B.L. Anla (Food Tech., Mysore)
2. Michal Dow (Biochem. NAS staff)
3. E.R. Pariser (Food Tech. MIT)

Peserta :

1. Purwo Arbianto
2. Hardiman
3. Suhadi Hardjo
4. Nasruddin Iljas
5. Sofyan Ilyas
6. Siti Isnijah S.P.
7. S.B. Joedono
8. Komarjani
9. Musrofinah Mahlan
10. Suwarto Martosudirdjo
11. Dian Maulida
12. Sidik Moeljono
13. Sjahnian Muhyi
14. Muslimin Nasution
15. M. Anwar Nur
16. Nuryadi
17. Redyowati
18. Atjeng Muchlis Syarief
19. Soedito
20. Sjafar B. Sinambela
21. Darjo Somaatmadja
22. Ig. Suharto
23. Ismu Sukanto Suwelo
24. Susaroono Wijandi
*25. F.G. Winarno (M.S., Ph.D.)
26. Winoto.

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* Vice-chair of the Conference

Contacts
Overseas to
visit

Notes

1. 10 % of attendees are from LDCs
2. Two workshops held - Massachusetts & Washington D.C.
3. Two background papers prepared - being edited.
4. No projects written
5. Contacts to go overseas to visit LDCs in Jan
6. Contacts asked if Regional (Nutritional) Bureaus had been contacted in overseas ~~offs~~ offs - they said no
7. Belis said it would be more difficult to implement human nutrition project overseas.
8. ~~Bree~~ Brosseau, Guatemala not being used at LACAP - he is working with better
9. Fitzgerald - his nutrition person from NEast has given LCAD 8
10. Nov 7 & 8 } Calloway & (Calloway)
Dec 12 & 13 } Pam Kahn will contact
Fred on her appearing
before JRC & give
report of his planning
grant