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FUNCTIONAL SIGNIFICANCE OF MARGINAL NUTRIENT DEFICIENCIES: PROGRAM-PROJECT PLANNING

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THIRD QUARTERLY REPORT ON THE FUNCTIONAL SIGNIFICANCE OF MARGINAL NUTRIENT DEFICIENCIES

Workshops on Intake and Function

The workshops on intake and the five aspects of function were held as specified in the second quarterly report. A thorough summary of conclusions from the first four workshops was written for the fifth (Social Competence) by one of the participants, Leonard Joy, and is quoted below.

Conclusions from the first four workshops: These notes attempt to provide an overall view of the conclusions reached on the following matters:

- Research objectives;
- Research priorities;
- Research methods.

The purpose of these notes is to inform the 'Social Competence' workshop of relevant earlier discussions. In this context, earlier discussions are seen to be relevant where they bear on matters of 'Social Competence'. In addition, however, since this present workshop has assumed a function of reviewing the coherence of the overall program, matters which relate to this issue are also presented.

Research objectives: All groups were presented with the overall objectives described by AID. Two groups (Disease and Cognitive) chose to elaborate these. Both emphasized effective conceptualization of the nature of the interrelationship between variables resulting in impairment as a prime research objective. This necessarily included the identification of relevant variables. Research would proceed to establish the validity of the hypothesized links by the elucidation of process and its growing/governing mechanisms and, thence, by attempts at quantification. Both 'Disease' and 'Cognitive' were concerned with focusing research towards an understanding of the prevention and amelioration of impairment and 'Disease' argued that 'the final test of the hypothesis should be conducted in a setting that would have relevance to eventual operational programs' (DS) in order to pursue the objective of improving planning for the ultimate improvement of human health.

Research priorities: Two of the workshops listed gaps in knowledge and questions which needed to be answered. (Reproduction p. 3-4; Work p. 3-4). Since reproductive, rearing, and work competence relate to social role competencies, all the 48 items listed may be seen to relate to 'Social Competence'. Some, however, do so most directly, e.g. "Do changes in energy intake affect absenteeism and turnover of the workforce?"

Overall, however, the issues which seemed to emerge, more or less explicitly, as major gaps in knowledge were those regarding the long term effect (as in, possibly: malnutrition, poor lactation, poor maternal performance, poor imprinting, poor second generation nurturing) and the ramifying social effects

(as in, possibly: malnutrition, reduced social and work activity, poor productivity, low food output, inability to support family, breakdown of other social roles, weakening of wider social networks and institutions). It was clear, however, that while such long term and ramifying effects could be hypothesized in general, more work was needed even to formulate these as specific hypotheses.

In attempting to establish priorities for research the 'Reproduction' workshop proposed as criteria that:

'1. The problem associated with the research area should be both serious and widespread;
2. There should be significant potential for applying research results to government policy or practical programs;
3. The research should promise to be cost effective.

Similarly, the 'Work' group proposed as criteria that,

1. Efficient use is made of available knowledge.
2. Questions are addressed which when answered, can give rise to practical, locally relevant solutions for improvement of energy nutritional status.
3. The project when launched has a high probability of being completed.
4. Appropriate utilization made of qualified local manpower.'

The only other group to make an explicit statement about criteria to be used to identify priorities was 'Cognitive'. This group argued that it was 'especially important that the available resources be directed towards the problems for which the solutions have the greatest potential for improving the quality of life'. (p. 11).

The 'Disease' workshop avoided specifying priorities in terms of specific intake-disease relationships to be studied. Indeed, it is not clear from the report of the meeting that intake-disease relationships would necessarily be studied with respect to specific diseases one at a time. Instead of specifying priorities in this form the group proposed what it called 'specific research objectives' which were:

'1. To develop a functional classification of nutritional status as it relates to expression of disease.
2. To determine the relationship of nutritional status to vulnerability to stress and/or disease expression.
3. Identify the specific contribution of total food intake to nutrition status.
4. Establish the validity of the linkages in the total system that relates food intake to disease.' (pages 3-5). (These headings need to be read in the context of the full report.)

The 'Cognitive' workshop also avoided the question of priorities and spoke in terms of 'research needs' which they listed as follows:

1. Interrelations between nutritional and socio-environmental influences on intellectual functions.
2. Aspects of cognitive likely to be affected by changes in nutritional status.
3. Reversal of cognitive deficits.

These headings were elaborated (pages 5-12) and several specific questions were listed for attention (e.g. 'Does the malnourised child's physical appearance affect the care giver's response to the child?') which have potential relevance for 'Social Competence'.

While several illustrations were given of specific relationships of potential interest none of these was singled out for priority attention. However, attempts to single out the effect of intake from socio-environmental factors were rejected in favor of studying the combined effects of all such factors. (p. 6).

The workshop on reproductive competence identified as priorities:

'1. The relation of maternal nutrition to the quality, quantity, pattern, and duration of lactation.
2. The relationship of patterns of weight gain during pregnancy to pregnancy outcome, specifically complications of pregnancy and low birth weight infants.
3. The timing and characteristics of supplements of human milk with regard to lactation and the health of the child.
4. Significance of weight at birth.
5. Effects of pregnancy and lactation on maternal nutritional and reproduction status.
6. The effect of family planning on lactation and maternal and infant health.'

As in the other groups these headings are elaborated with specific examples of more detailed questions. (pages 7-12).

Finally, the workshop on 'Performance and Work' proposed as research priorities the questions:

'1. What critical levels of energy intake enable individuals to perform different activities?
2. Does nutritional status of an individual in childhood affect that person's work capacity and physical fitness as an adult?
3. To what extent do levels of performance capacities relate to physical activity and work output?
4. Are there differences in the activities performed at different habitual energy intake levels (i.e. in the behavioral profiles of the community) and what are the consequences for the individual, family, and community?'

This last heading is clearly a 'Social Competence' issue. The headings were not elaborated.

Research methods: All previous groups have noted that the aspect of human competency under their consideration was closely linked to aspects discussed by other groups. While little attention was given directly to the question, even the links suggested by the group reports indicate that we are dealing with a strongly interactive system. This might be further examined by entering the expected degree of relationship in the following table: (Entries depend on level of deficit assumed.)

	Disease Response	Cognitive/ Sensory Development	Reproductive/ Rearing Competence	Work/ Productivity/ Activity	Social Competence	Intake
	AFFECTS					
Disease		?	?	?	XX	XXX
Cognitive	XX		?	?	?	XXX
R/R	XXX	XX		?	XX	XXX
Work	XXX	XX	?		XX	XXX
Social	XX	XX	X	XXX		XX
Intake	XX	?	?	XXX	XX	

While the entries showing the strength of relationship are national and make implicit assumptions that should be explicit, if such a pattern as is shown were to be validated it would reveal a very strongly interdependent system. This has major implications for research design recognized by all groups and stated by the 'Disease' workshop: '... research relating to two or more functions might be conducted with the same populations at the same time, perhaps with considerable economy, and with increased interpretive benefit'.

However, it is recognized that if the populations under study are relatively small (say, village or small island communities), or if it is found necessary to use small samples which are to be subjected to several aspects of investigation, it is readily possible to overload the people under investigation--imposing on them an inordinate burden and risking poor response to investigations.

What is critical here is precisely the nature of the burden placed on respondents and the severity of the burden placed by the breadth and depth of the study. Since there is a limit to the burden, that if it is reasonable to impose, breadth can only be achieved at the expense of depth and vice versa.

It was noted above that a prime task was seen to be the elucidation of the variables and the patterns of interaction between them. This then needed to be followed by attempts to conceptualize the mechanisms and processes of interaction prior to the determination of key relationships for quantification. It seems unlikely that such investigations as this would require imposition of a heavy burden on a community. At the next stage of quantification and testing the choice of relationships for investigation would need to be made so as to balance breadth with depth and, by care in sample design, so as to spread the burden of investigation through the population.

Generally, the groups envisaged that studies would need to be community specific. (The 'Disease' group especially considered criteria for selection of communities.) However, the 'Disease' group, especially, spoke of a 'research continuum' and recognized that community level investigation might well identify and prompt required research in the laboratory or human metabolic unit.

All groups were conscious of the influence of culture upon the relationships to be examined. This was seen to give rise to several problems, especially:

1. The problems of identification, definition, and quantification of cultural variables;
2. The problems of designing different studies so as to allow cross-cultural generalizations.

The identification, definition, and quantification of variables was seen by all as a major problem for hypothesis testing and for the quantification of relationships. Most competence functions present difficulties. They pose problems too, with regard to the choice of standardized definitions and measures (which might prove inappropriate in specific cases) and ad hoc definitions and measures which would frustrate generalization. Suggestions were offered of possibly relevant variables and potentially useful indicators. (Disease p. 17-18, 29-30; Cognitive p. 12-18; Reproduction p. 7-9, 12-15; Work p. 6-8, 10-12.) Proposals for research approaches came from three methodologies: 'statistical experimentation and control', 'epidemiological' and 'inquiring systems'. These were not seen to be mutually exclusive; indeed, they were seen in some reports to be complementary, with statistical and epidemiological methods

as part of, or stemming from, a systems approach. This view implied research designed in phases--each phase, after the first, being designed from the results of the preceding phase.

In the presentation of the 'Disease' workshop, the systems approach is seen to have particular value in elucidating socio-biological interaction mechanisms and in generating hypotheses about these. The statistical and epidemiological approaches are seen to be most useful for testing and quantifying hypotheses. The possibilities of proving or quantifying interrelationships are not always assumed and the 'Disease' report emphasizes that the failure to establish a relationship by statistical methods should not be taken to mean that the relationship does not exist or is not significant. (p. 28).

The workshop on 'Social Competence' produced some strong points, particularly in the area of ethics, but no clear research priorities were defined. This is a result of the fact that there is an extremely limited research base in the literature on the subject of the relation of nutrient intake to 'social competence' and therefore it was not appropriate to consider research gaps (the whole area is a gap) and try to establish research priorities. Only examples of possible research topics were put forth. It might have been a more profitable workshop if one or a series of working definitions of social/societal competence had been developed. It appears that a first phase of the CRSP might focus on the societal impact of mild/moderate food deprivation as expressed through functional deficits in the disease, reproduction, work/physical activity, and cognitive/sensory development domains with a second phase exploring social competence in a more structured research style. Further consultation with experts on the subject of social competence is taking place presently.

Appendix I contains lists of the participants and the reports from each of the five workshops. An integrated version of these reports is now in preparation and it was found that the sections on research priorities were particularly important to this compilation. Since the first workshop on disease did not address this topic directly, a letter was sent to the participants requesting their thoughts and recommendations. Appendix II contains a copy of this letter.

Steering Group Meetings

The first steering group meeting was held September 29-30 in Boston. Background information about the program was presented and the role of the steering group discussed. At that time, responses had been received to the original 'Notice of Research Opportunity' and it was concluded that it would be impossible to make objective evaluations of the institutions on the basis of this response (curricula vitae of interested investigators) and a questionnaire should be devised to elicit the appropriate and necessary information. Eight criteria for institutional evaluation were put forward; they are listed in the minutes of the meeting in Appendix III.

The second steering group meeting was held December 17-19 in Berkeley. The purpose of this meeting was to evaluate the institutional responses to the detailed questionnaire (the questionnaire and cover letter are discussed in the next section of this report). The formal criteria used for evaluation were the following:

1. Ongoing research should be directly and clearly relevant to this collaborative research program as presently envisioned, including orientation toward human research and problems experienced in less developed countries.
2. There should be considerable experience in and linkages with less developed countries and evidence in the form of published papers and reports that past associations have been productive.
3. There should be evidence of the required range of competencies in each program area proposed, or indications that such arrangements would be made (consultants, etc.).
4. The principal investigator should have sufficient time available to devote to this program, in light of competing commitments.
5. The institution (or group of institutions) has the capability to carry out research in several or all designated program areas and evidence that the proposed investigators can form a coherent working team.

A final list of institutions meeting at least four of the five criteria (with criterion number 3 mandatory) was produced and it is hoped that these

institutions (and aggregates thereof) will submit complete proposals covering most or all of the program areas. It was decided, however, that no institution should be excluded from submitting a complete proposal and this was reflected in the letter which will be sent to all responding institutions (letter discussed in following section). Members of the steering group prepared lists of potential reviewers for the research proposals and they discussed ethical issues of the CRSP. Minutes of this meeting are included in Appendix III.

U.S. Institutions

As mentioned above, a set of forms was sent to each interested institution in order that a more objective determination might be made regarding institutional competence for this program. The cover letter, a copy of one set of forms, and the list of the institutions and the program areas in which they indicated interest is to be found in Appendix IV. The forms require a listing of six current research projects with direct relevance to this program, techniques used, and facilities available. A description of past and present linkages with less developed countries was required along with evidence (publications and reports) that the linkages were/are productive. One principal investigator for the project was to be chosen. It was decided (by the steering group) that certain disciplines should necessarily be represented in a team proposing to do research in any of the five areas. The disciplines were the following:

Human Nutrition
Nutrition, Other Relevant
Quantitative Population Studies
Social Sciences
Behavioral Sciences
Biomedical Sciences
Design and Statistical Analysis
Data Management

Name, title, and principal methodologies used were to be submitted for each member of the proposed team.

The cover letter stated that these forms would be used to narrow the list of potential participants; that isolated individuals could submit the forms; and that there ultimately would be a matching funds requirement.

The final list of institutions thought (on the basis of the questionnaire) to be competent to conduct the research includes the following:

All/Most Research Areas

Columbia University
Cornell University
University of California
University of North Carolina/
North Carolina State University

One-Three Research Areas

(I. disease response; II. reproductive competence; III. work output and physical activity; IV. cognitive and sensory development; V. social competence.)

Iowa State University (I,IV)
Pennsylvania State University (III,V)
Purdue University (I,II,IV)
Tufts University (V)
Tulane University/Medical College of Wisconsin (II,III)
University of Arizona (I,II)
University of Connecticut (II)
University of Kansas (I,IV,V)
Vanderbilt University (I)

A copy of the letter to be sent to all responding institutions is contained in Appendix V. It includes the above list, but does not exclude the possibility that other institutions may submit complete proposals. All proposals received will be read by at least three reviewers (a nutritionist, an epidemiologist, and an expert in the program area) and finally by the steering group before any recommendations are made to USAID.

Forthcoming Meetings

A sixth workshop will be held January 15-17 in New Orleans. It is composed primarily of nutrition and related research experts from lesser developed countries and the purpose is to obtain their views and suggestions on the results and priorities of the five workshops, the feasibility of the research in their countries, their opinions of the program objectives, and tneir own priorities for this research. The participants will be the following:

George Beaton, Chairman (Canada)
Doris Calloway (UCB)
Edouard de Maeyer (WHO)
Hekmat El Sayed Aly (Egypt)
Carmen Hamann (Brazil) (cancelled)
Paul Lunven (FAO)
Jose Obdulio Mora (Columbia)
Achola Pala (Kenya) (cancelled)
David Perera (Sri Lanka)
Marian Radke-Yarrow (Steering Group)
Giorgio Solimano (Chile)
S.G. Srikantia (India)
Aree Valyasevi (Thailand)
Christina Wood (UCB)

APPENDIX I

PARTICIPANTS AND REPORTS OF FIVE WORKSHOPS ON INTAKE AND FUNCTION

DRAFT

REPORT OF WORKSHOP ON NUTRIENT INTAKE AND DISEASE RESPONSE
SEPTEMBER 25-29, HYANNIS, MASSACHUSETTS

1.) Background

A workshop convened by the Food and Nutrition Board and its committee on International Nutrition Programs considered the need for a functional definition of nutritional status (1). The consensus of the workshop participants, drawn from a broad spectrum of relevant background experiences and interests, was:

i) There is strong reason to accept the premise that severe malnutrition is associated with impairment of a number of human functions.

ii) There is uncertainty about the relationship of less-than-severe ("moderate" and "mild") malnutrition to these functions. There is no clear information about the level of nutritional status that makes the beginning of impaired functional capacity or whether the response is linear or curvilinear.

iii) Because of the immensely large populations affected by less-than-severe malnutrition and because of the potential importance of its sequelae for individuals and for society, these relationships must be understood.

iv) Information on these points has relevance to anyone engaged in the consideration of intervention programs.

Although the workshop noted that certain functions may relate most closely to certain specific nutrients, and that nutrient-nutrient interactions were possible, attention then and since has occurred upon the relationship between general undernutrition and function.

The Workshop identified five broad areas of human function which might be particularly relevant to those involved in food, nutrition and health planning. These were: 1) disease response; 2) reproductive competence; 3) work output; 4) cognitive function; and

5) social and behavioral function.

Under Title XII, USAID has assumed responsibility for funding research in this area of human nutrition. The above five functional areas were designated as topics to be explored in a series of planning meetings. The present workshop was convened to consider the first of these areas and to offer advice on research approaches that might serve to investigate the relationship between food intake and disease response in an expeditous and quantitative manner. The participants recognized that in actual implementation, research relating to two or more functions might be conducted with the same populations at the same time, perhaps with considerable economy, and with increased interpretive benefit. Nevertheless, discussion was focused on the one area of function on the assumption that decision on combining areas of function in research designs would be taken later.

The participants were acutely aware of the fact that this challenge was not to decide whether or not relationships existed between food intake and disease response but rather to design studies that might describe these relationships across varying ranges of food intake and across varying degrees of less-than-severe malnutrition in quantitative terms.

2.) Objectives of the Research

The background reasons for considering this area of research have been set forth in section 1. To provide a basis for considering research design, the actual objectives of the research were defined more precisely.

Overall Objective: To determine the relationships of food intake to the expression of disease in the community.

For the purpose of this study food intake is expressed primarily in terms of energy intake. It is recognized that when food intake is

low, the intakes of nutrients may also be low and that disease effects attributed to low food intake may not be consequences of inadequate energy intake per se. It is also recognized that at levels of food intakes that satiate total energy needs there may still be marginal or inadequate intakes of specific nutrients. These possibilities will warrant consideration in experimental design and data interpretation. They do not distract from the underlying question, does total food intake relate to disease expression.

Study design must take into account also the fact that food intake is only one of many variables that may affect disease expression. These other factors must be "controlled" or taken into account in statistical analyses if the objective of describing the contribution of food intake is to be achieved. Social changes and behavioral changes taking place during the study cannot be ignored.

Finally, it is emphasized that what is sought is not a "yes/no" answer but a quantitative description of the relationship between a range of food intakes and diseases in the community. Obviously this imposes special demands upon the design and analytical approaches

> Specific Objective 1: To develop a functional classification of nutritional status as it relates to expression of disease.

This may be seen as an objective in its own right and as an intermediate stage in the examination of the relationship of food intake and disease expression. The primary focus would be assessment of nutritional status with regard to the adequacy of the energy balance, both short term and long term. However, it may be appropriate to include other parameters of nutritional assessment, particularly where it is suspected that inadequacies

of specific nutrients may be confounding variables in data interpretation.

> Specific Objective 2: To determine the relationship of nutritional status to vulnerability to stress and/or disease expression.

Again this may be seen as an intermediary stage that would both add credibility to the overall relationships that might be observed and provide information about mechanisms. If indeed it is possible to identify parameters in the host that reflect both nutritional status and vulnerability, the research may result in better indices of nutritional status. Considerations should be given to measures of vulnerability that have been shown to be sensitive to mild and moderate degrees of food deprivation, and to relate closely to disease expression. Of particular interest in this regard will be parameters of the immune response.

> Specific Objective 3: Identify the specific contribution of total food intake to nutritional status.

The aspects of nutritional status that are of interest are those which may relate to vulnerability, and those which may be necessary in order to control for confounding specific deficiencies, where there is thought to be a problem*. The design and analysis of research in this area will have to take into account the contribution of other factors associated with the biological and social

*Some micronutrient deficiencies which seem likely to occur in certain settings and be confounding variables: Iron, zinc, vitamin A, folic acid, riboflavin, pyridoxin, thiamin.

environment which may affect this relationship.

Specific Objective 4: Establish the validity of linkages in the total system that relates food intake to disease.

If the research design follows a phased approach in which component linkages are examined (eg. the specific objectives outlined above) then it will remain necessary to test the hypothesis in the total system--that is the examine the relationship between food intake and expression of disease in the community. Since the underlying objective of the research is to provide information relevant to planning and ultimate improvement of human health, it follows that the final test of the hypothesis should be conducted in a setting that would have relevance to eventual operational programs.

3.) Research Design

In considering possible approaches to achievement of the above objectives, a number of potential designs have been considered. It is to be recognized that there is a continuum of research endeavors that relate to ultimate applied goals, relating to the improvement of the nutritional health of human populations. This continuum may be considered in terms of types of research in a sequence of stages (see table 1) which might normally follow one from another. As new information arises in the basic science laboratory, or in the fundamental studies of the social scientist, it gradually finds its way into the design and conduct of research at a more operational level. Questions arising at the level of applied operation may in turn provide stimulus for basic studies.

TABLE 1: RESEARCH CONTINUUM*

Studies in this column are planned experimental (intervention) studies	Observations	
Test tube research Animal studies Clinical metabolic studies	Clinical Experiments of Nature (i.e. patients present with critical defects and symptoms which can be studied)	Descriptive Epidemiology: -Is gradient of A (putative case) across populations associated with gradient of B (outcome)? Systems Analysis: -How do gradients of different A's and their interactions correlate with (predict) gradients of B? Analytic Epidemiology: -Fortuitous experiments of nature (cohort studies)--Is there a gradient of B in those who were exposed to A? Case-control study: -Were those who now have B previously exposed to A? Experimental Epidemiology Study in Individuals: -Does B change in individuals as A is changed in individuals? Experimental Epidemiology Study in Communities: -Does the mean of B in a community change when A is changed across communities?

* Public Health programs are not considered suitable for research on this topic. They may grow out of the results in the future if benefits are shown by the techniques listed above in a logical staged manner.

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In considering the objectives of the present research, it is clear that the required investigation is at the level that might be called descriptive and analytic epidemiology and systems research. At a later stage, to establish causality in the described relationships it may be necessary to perturb the systems through experimental epidemiologic interventions.

Three broad approaches to the research design are outlined below together with assessments of their probable strengths and weaknesses and potential advantages and disadvantages.

SYSTEMS APPROACH

1. Why?

Even the most direct physiological linkages between nutrient or energy intake and vulnerability to disease are not isolated, whether present in individuals or in communities. Rather they occur as parts of larger ecological systems which can be described and illustrated, as shown in the accompanying figure. Therefore it is essential in the development of a strong study design, to possess sufficient understanding of the larger system to sharply focus the particular research questions. Since answers are likely to come piecemeal, and final confirmation may require an intervention study, it becomes imperative that the research design be finely tuned for answering specific questions, which will permit quantitative assessment of the hypothesis. Definition of the system has a second purpose. The system may reveal additional subjects of interest, such as the delineation of causal links and may identify areas for intervention which

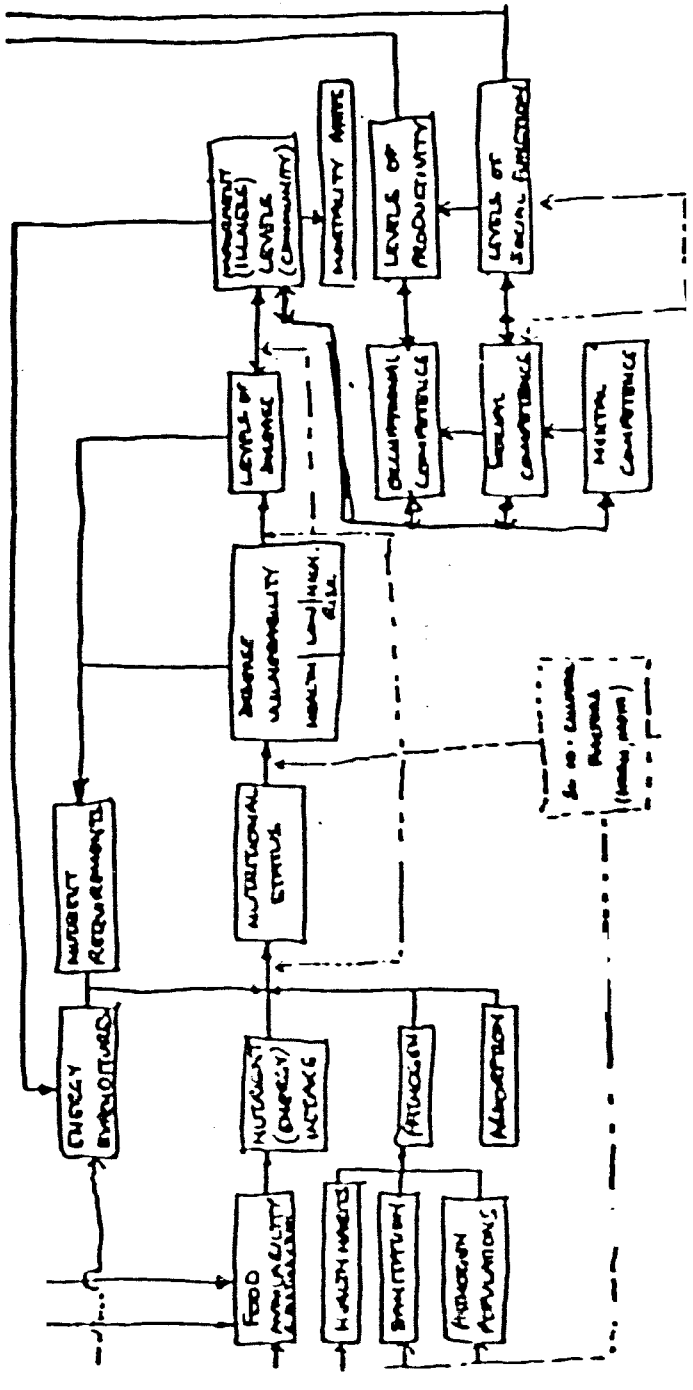

Figure 1:
An example of a "systems map".

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were previously not suspected. This process is also necessary for the structure of a system of evaluation of the relevance of choices over time.

2. What?

The systems approach can be expected to provide two principal forms of guidance in research design: a. identification of key variables in the community from the perspective of both the investigators and the subjects, with estimates of the range and level of importance of these variables; and b. a conceptualization of the relations between these variables in both biological and sociocultural terms. Of unique importance is the definition and estimation of the repercussions of disease in one individual on other members of the community.

3. How?

Through collection of demographic, ethnographic, biomedical, morbidity and mortality experiences of the community a working assessment of the nutritional intake—disease vulnerability linkages is made. This is not intended to be exhaustive or incontrovertibly authoritative, but rather to be a broad brush outline of the key features of the group. From this, judgements can be made as to the identity of the significant problems, and the likely sorts of stress which make previously inapparent disease suddenly manifest. These problems can then be given prominence in the study design by a higher focus analysis of the physiological functional systems involved in the particular source of identified disease risk. These systems are studied in terms of both baseline function, and functional reserve under applied stress, along a scale of vulnerability from that existing when there is

optimum nutrient intake, to that of high risk (pre-disease) (figure 2).

4. What Might the Approach Mean in Practice?

After the community has been selected the first step would be to obtain available information on the community, eg. climatic, demographic, socio-economic, farming system, health care, morbidity, etc. field work would be done by a cross disciplinary team, eg. an epidemiologist, anthropologist, and agricultural economist. Initially, a "feel" for the village, i.e., its demography, social structure, economic differentiation, diet patterns, and sanitation would be obtained to gain a preliminary view of the nature of nutrition and disease problems, including their incidence in different sections of the community, and their perception by the people themselves.

On the basis of this broad view detailed case studies would be done of households from differnt sections of the community. The focus of household case studies would be on identification and appraisal of nutrition and disease problems, and an assessment of their significance to the household. Questions such as "how does behavior of the household change to reduce its nutrition and disease problem?"; "Why is behavior not already modified in this way?"; "What would it take to change behavior (farming practices; food selection, purchase, preparation; hygiene, etc.)?"; "To what extent, and with what significance, could behavior change within the household to reduce the severity of its nutrition and disease problems?" would be asked. Complete tabulations for each member of the family from observation or estimate of such data as age, sex, height, weight, food intake, energy expenditure, health status, and

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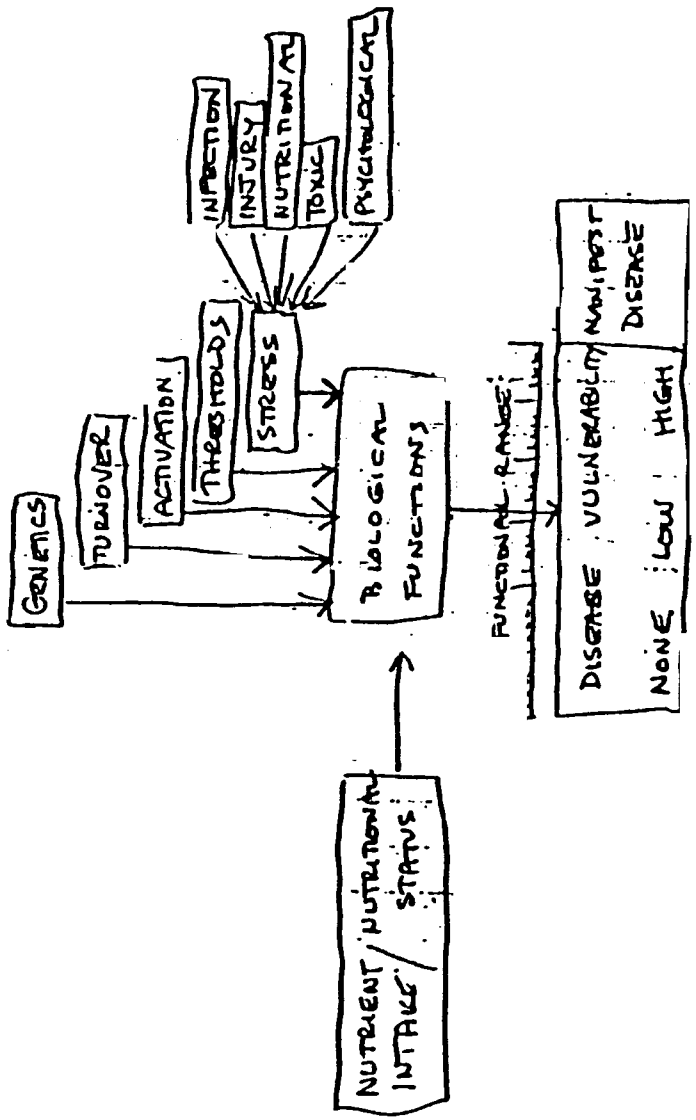
Figure 2



disease history would be obtained. Such tabulations would represent, in matrix form, information on variables serving as indicators which relates to the elements of a 'systems map' (figure 1). For each individual causal links would be postulated between intake, nutritional status, disease and impairment. Links would also be traced between individuals to identify, for example, how one household member's infection becomes another's stress or his/her incapacity for work, or nursing, results in another's low intake. An assessment of these links will provide the basis for assessing the significance of nutrition and disease impairments within the household.

The community as a whole can be viewed in a similar way. For example one might ask "in what way can nutrition related disease be reduced by changes of behavior within the community?" "Which aspects of the communities nutrition and disease problems would be most important to attack?"; "By what measures?"

At this point there might be some uncertainty about a variety of matters for example, the number and nature of people (socio-economic category) affected by specific nutrition and disease problems. The contributions of nutrition and disease impairments to subsequent and wider impairments effected through different pathways (eg. impairment affecting farm output, food availability, food intake and food intake as it affects duration and extent of impairments). Conceivably, this uncertainty might imply further uncertainty about matters such as the significance of disease impairments, at what points of the system intervention would be most effective, how far "packages" of measures will be necessary, and so on. Decisions will then be required as to what

information will improve confidence in the identification, design, and assessment of interventions and whether the cost of obtaining such information, including expenditure of the time will warrant collection instead of proceeding directly to the design and implementation of an intervention.

In the event that more information and understanding is necessary, the next phase of work might range from simple survey work, to an epidemiological cohort study, to comparative case trials to laboratory, or metabolic unit research. Whatever work is indicated, its purpose and application, the degree of accuracy required, and the type of information required will be clearly defined. The design of the study--or studies-- will be specified accordingly. The results of the research will as a result have immediate application, and will lead to the identification of relevant problems and design of appropriate interventions.

AN EXAMPLE OF AN EPIDEMIOLOGIC APPROACH

Introduction

This example represents one epidemiologic method which might be used to produce guidelines for research on the relationship of food intake to the expression of disease in communities. There are many valid but different ways to approach such research. This section will discuss some of the ways in which epidemiological research can be of value. Epidemiological studies can be divided into descriptive, case control, cross-sectorial and cohort studies. The availability of resources, the questions to be answered, and the populations to be studied will determine which of these methods should be used to answer the research question.

It is likely that descriptive and cohort studies will be of the greatest value, that cross-sectorial will be of little value, and that case studies may be advisable in special circumstances.

The bulk of this report will describe the use of the cohort approach, because of time constraints and because we believe that it will be usually the most effective of the epidemiologic methods in this research. This does not imply that there will be a bias against proposals using other epidemiological models which appear to have characteristics needed for success. In any case, many of the statements made in the methods of procedure section apply to all types of epidemiological studies which are likely to be proposed.

The Cohort Approach

For the purpose of this section an epidemiologic cohort approach to the hypothesis that nutrient intake as measured by energy is is inversely related to disease production in the community will be discussed. It should be understood that while in this example the independent variable could be measurement of nutritional status, level of sanitation, medical care availability,etc. In more complicated designs combinations of these variables could be tested. While such designs would add to the cost and complicate the analytical problems. This could be done if necessary for achievement of the research objective. Such designs could prove to be necessary if the respective contributions of these latter variables are a part of the assessment of the relationship. For our purpose a cohort approach which relates the independent variable at several

discrete levels of magnitude, or as a continuous function, to outcomes, as disease expressions, is proposed. Actually the design is not only a prospective approach, but embodies a longitudinal component, in that both the independant and dependent variables will be re-measured at pre-determined intervals, taking season changes into consideration. This will provide not only for surveillance of dietary changes but, if the intervals are not too long, for a disease surveillance capability of greater reliability. Food intake measurements will also be made more reliable.

Method of Procedure

A. Selection of communities and their descriptions (see page discussion of community selection).

1. Several communities should be selected in order to insure range of variability in the independent variables, and repli- if unforeseen complications prevent execution in each.

This is necessary because the initiation of a major long term study in only one or in too few communities creates an unacceptable risk, that an unexpected event in a community may compromise or destroy the entire study. If possible one shall be prepared to capitalize on unexpected events. Furthermore, if a greater number of communities, which will ultimately be compared on a number of other variables are enrolled, a broader range for gradients of intake will be assured.

a) In this design communities hasll be selected prepresenting magnitude of disease incidence or prevalence in accordance with available data. Every effort shall be made to verify the data using available information from all relevant sources, including local health centers and ministry

authorities. An range of magnitude of disease occurences amoung these communities will assist in ascertaining whether the relatioships, if found, hold over the range of disease magnitude.

b) Communities selected will have demographic, environmental and social attributes, such as size, population distribution of age and sex, sanitary status, and availability of medical care which are comparable. Note, if a design is suggested which includes assessment of variables contributable to the disease states, then the communities should have a range of such variables, albeit the population to be studied should be increased.

c) Since the diseases which may be related to nutrient intake could also be related to sanitation and available medical care, these variables must be included in the study, and efforts should be made to select communities in which socio-economic status is not so disparate as to relate disease to affluence, particularly the possession, for example, of water supplies and sewage disposal facilities or access to medical care. It is recognized that in populations with divergent food energy intakes it is likely that high intakes will often be associated with increased wealth. However, it is not necessary that small differences in affluence which alter energy intakes, must also alter other variables thought to be related to disease expressions. It will be the responsibility of investigators either to select communities in which confounding variables such as these are at such a low level that the study is not compromised or to suggest methods of controlling on these variables.

c) Because the study will be prospective in design and will require a reasonable length of time, and since spin-off or continuing research may be indicated, it will be desirable that reasonable evidence or continued cooperation and stability of the community is available.

d) Reasonable assurances of community participation should be obtained by the applicant researcher before submission of applications.

f) There should be no other conflicting research or other promotion of health activities in the community, or nearby communities which might interfere with the execution of the research design.

g) In many case communities in which other studies have been conducted may be of special value because of an accumulation of available information which will be helpful in the conducting of the research. However, it should be cautioned that communities should be avoided in which previous studies have failed because of lack of cooperation or in which there is reason to suspect that cooperation in a new investigation may be affected by the population's fatique at being overstudied.

B. Approach to Nutrient Intake

1. The measurement of nutrient intake shall take the form of quantitative and qualitative dietary surveys of food consumption by families and individuals in the study population.

2. An adequate sample of the community population, properly representative of the demographic characteristics of the populations shall be drawn and surveyed for such intakes.

3. Nutritional status as measured by appropriate standardized historical, anthropometric, clinical and laboratory methods shall be part of the initial survey and at selected intervals thereafter. The specific nutritional methods chosen will depend on the hypothesis tested, It is possible that by serendipity, or design, the data obtained from this type of study may permit analysis of such a nature that comparisons between disease expressions and other independent variables such as nutritional status may be made.

Measurement of the Dependent Variable--Disease Outcomes.

1. A surveillance system for disease events and prevalence will be a vital component of the design.

2. All morbidity shall be recorded irrespective of whether finite diagnoses have been made by health centers or visiting health personnel, or the illnesses are undiagnosed but recorded as selected signs and symptoms. A method of validation shall be proposed. Validation of many of these illness events may be derived from health centers and schools.

3. At the intervals of re-examination of dietary intake and nutritional status such records shall be assembled, validated and collated for systematic retrieval. The interval examinations of nutrient intake, nutritional status and the collection of intervening illness data shall permit time series analyses of the interrelationships between these events as well as a measurement of possible feedback mechanism.

D. Analysis

The appropriate analyses will be contingent upon the method of sampling and the precise form in which the data are collected. However, the outcomes shall not only be total morbidity (and mortality) but discrete disease entities or

constellation of signs and symptoms.

E. Pilot Study

It is obvious that before embarking on the full field study the methodogies should be tested with a small scale pilot study. Evidence of the validity of the instuments to be used shall be demonstrated either by the investigator's previous experience or by such a pilot study.

EXPERIMENTAL EPIDEMIOLOGIC INTERVENTION STUDIES

1.) Intervention studies are very complicated and involve ethical considerations therefore they should only be performed when information from other sources gives evidance that the hypothesis to be tested are likely. One kind of evidence relates to the elucidation of mechanisms (linkages) between dietary intake and disease expression, from animal and clinical experiments. A second relates to the finding of overlapping positions of these linkages in man. An example is the relation between nutrition in pregnancy and infant morta lity. Documentation available for energy effects are birth weights. Widespread evidence that birth weight is associated with infant mortality equals two overlapping links. The total chain now needs to be documented. The third linkage relates to the magnitude of the problem, i.e. prevalence or incidence of the particular type of malnutrition and the likely proportion of illness or death due to that malnutrition.

2.) Intervention should be as simple as possible. For example, unless non-additive interactions are likely between various interventions, only one intervention and its controls should be tested.

3.) The deficiencies and interventions being examined must be

appropriate for the community being studied. For example calories are unlikely to be limiting in obese women. This requires:

a) Careful baselinge observations of study populations

b) Testing of nutritional interventions and control interventions under carefully controlled considerations for safety and effectiveness,

c) Pilot testing of interventions in similar communities to assess acceptablility and the extent of replacement.

4.) One must be able to identify the effect of the intervention separately from the effects of all other (confounding) factors. This is done by:

a) Randomization of interventions or matching,

b) Use of appropriate controls such as:

i) Placebos (in some circumstances ethical considerations will not allow)

ii) Individuals as their own controls and cross-over designs

iii) Double blind assessment (blind assessment may be difficult with macronutients)

5.) When interaction of interventions is not sought there should be a clear description, or experiment control of the major confounding variable on disease. For example:

a) In a study of measles as an expression of nutrition, measles antibodies should be measured in different intervention and control groups, either to mathch for analyses or to assure that induction of treatment was random

b) In study of febrile illness, immunization against epidemics

which strike comparison communities arbitrarily but not at random, and could destroy comparibility. (Note: Not every putative confounding variable cannot be measured. A strong research design will identify the important ones, and randomize the others.)

6.) When possible "positive" controls should be designed to provide a relative measure of the intervention's effect. For instance, general health and environmental measures are thought to be measurably effective in affecting the outcome. If this is so, and nutrition intervention results in no effect, the latter findings is clearly not due to inadequate measure if outcomes (an important consideration in field studies) and even if present it may not be worth following up. Positive controls also control for placebo effects.

7.) When communities are the unit of analysis 3 to 4 for each kind and level of intervention is the minimum number of replications. Less than this number practically excludes studies of a gradient effect across communities.
Analysis of gradients of intake across individuals that do not control for self-selection, and other biases by experimental design will produce no better evidence than descriptive or analytic epidemiologic studies, unless the results are used to explain community effects. When community effects are so explained they aquire greater credibility.

8.) As many intermediary variables (linkages) between intervention and outcome should be measured as possible and the variables should all change congruently for the interference that intervention caused the outcome to be credible including the timing of the effects.

9.) The outcome measured should have a public health relevance for example death, observable disease, use of health care resource, etc.

10.) All results whether positive or negative should result in strong inference (power analysis).

SELECTION OF COMMUNITIES FOR STUDY

1. In general, community studies should be evaluated for their potential to produce information which will illuminate significant problems in our understanding of the interrrelationships between nutrient intake and dir : response. Studies should also be evaluated for their potential impact on the health and nutritional status of the communities under study.

2. A broad sample of communities and problems should be studied to cover a wide range of environments and social settings: rural and urban communities representative of particular classes of problems, comparable problems in different parts of the world, different kinds of problems within the same geographical areas.

3. Communities should be selected such that results will be broadly generalizable. Except where selection may illuminate some important general relationship between nutritional intake and disease it would be best to avoid communities with unique constellations of environmental-socio-cultural fearues, communities in the process of recovering from some prior disequilibrating stress (including previous interventions, natural disasters), and communities with reasonable likelihood of undergoing some major political-economic shock during the period of study.
Communities where prior interventions have taken place, though desirable from the point of view of having an extensive health

data base, should be judged appropriate only if the effects of the interventions can be deemed not to interfere with the collection of quality data necessary for proposed research.

5. Communities selected should be able to be compared in demographic, environmental and social attributes such as size, demographic structure, socio-economic structure, access to markets, access to state (health) services, etc. Depending on the specific research designs, communities must meet citeria of of size (large enough to grade research results, yet manageable, given project resources), homogeneity (differences where ralavent must be able to be identified and quantified), and feasibility (community structure is such that project can be executed in the amount of time envisioned).
6. In general, it is desirable to select communities from an area where ther is an existing data base on the subject of health and nutrition, to facilitate the preliminary research stage.
7. Projects should not be in competition with other health-related projects at the community level which might be disruptive to the community and investigators.
8. Communities should demonstrate potential for ongoing local participation in the project, and regional-national participation and cooperation of host country institutions shall be assured. It is desirable to locate projects where there is some assurance that local participants will benefit and where projects may have some impact on the state government's sensitivity to the need for further attention to problems related to health and nutrition.

ETHICAL CONSIDERATIONS.

Ethical considerations dictate that people should not be used as means alone. Further the participants must be able to give their informed consent to the study. This requires that participants understand the harms and benefits of accepting to participate and that they participate voluntarily. Harm maybe ethically acceptable if counterbalanced by benefits to the same individual and participation is voluntary.

Benefits may accure to oneself, one's family, one's community, one's country, humanity, science:

a) Individual--family--community: Possible benefit from intervention and assured benefit from other activities (eg. medical care)

b) Country--immediate applicability of knowledge (now always); training of indigenous workers and professional

c) Humanity, science, only if well done.

Harm may be limited to short term inconvenience; risk or harm but the possibility of long term inconvenience, risk, or harm exists and must be made explicit.

Voluntary participation: If short term need is high this will be a strong incentive to participation and short term risk will be acceptable; long term risk will be even more acceptible. This situation constitutes coercion. Therefore the receipt of program benefits (eg. medical care) must not be tied to participation..

If there is a minimum participation rate required to sustain funding a community will bring pressures to bear on individuals; thus the voluntary aspect is impaired. Benefit/harm ratio must be increased.

2. Relationship to indigenous scientific colleagues are an area of concern. Data collection is mining, whereas, data analysis, thinking, and processing add 'value'. Processing should be done with indigenous colleagues and they should be involed in research design and analysis. Data generated must be available to scholars in the country and also to international colleagues involved in the research.

3. Other issues to be considered are that:

   a) Health and nutritional (humanitarian) benefits should not be excluded from participants on the basis of research design.

   b) The existence of a scientific project in a community should not result in the exclusion of other benefits to the community which would otherwise have accrued to it, eg. environmental sanitation, electrification, family planning by government. Projects can ensure that villages remain comparable in spite of such introduction by insuring that introduction of such benefits is concurrant in all communities under study.

METHODOLOGICAL CONSIDERATIONS FOR RESEARCH DESIGN

1. Concepts of illness and health

   a). Cultural definitions and attitudes toward illness: Does the population uniformly label general syndromes as illness? Are differential rates (eg. male/female) of certain types of morbidity due to real differences in biological-medical terms or differential reporting? (Is it acceptable for males to be "ill" when they have the same symptoms as would be acknowledged as "illness" in women?)

   b). Cultural concepts of illness and health: In general, how do these affect illness reporting? What kinds of reporting

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of generalized syndromes (not necessarily labelled as "illness" in the culture in question) can best yield evidence on quasi-illness (possibly nutrition-related) states?

   c.) Cultural perception of basic problems, health-nutrition priorities: How do these illuminate problems, suggest research prioiities for cooperation?

   d). Culture beliefs, attitudes, and practices related to diet-illness: What pathways do they see between nutrient intake and particular classes of illness? What therapeutic dietary measures do they follow, conceptually and practically, for particular classes of illness (particular social categories)? How might these help establish research priorities or types of interventions or make interventions more acceptable?

2. Immune systems and disease

Emphasis is placed on the relationship between nutrition and infection, and studies commonly focus on the immune system as a functional indicator because it is seen as a protective system. Unfortunately what little evidence there is regarding immunollogical function in severe and mild malnutrition is not consistent. Some of the lack of consistency is probably due to variation in methods employed and their sensitivity, and in interpretation of changes noted. It is strongly emphasized that any proposal that involves immunological parameters as functional tests for nutritional state should be evaluated with caution.

3. Management and analysis of data

The usual fail-safe protection of the scientific community against improper analyses of data and incorrect inferences is the replication of the observations or the experiments. For large scale community data collection or experimental studies,

this repetion usually is not possible. The possiblity of incorrect analyses and inferences could be minimized by making the raw data available to the scientific-community at large. However this should be done only if privacy of subjects is protected and the investigators are given adequate time to do the important analyses themselves. Wider release of data requires better description of data collection techniques, documentation of the quality control for data collection, data file building, the presentation of distributions and summary statistics for each variable, and description of the data tapes to be released. New process control measures will be needed to assure that data are so presented.

Cautionary notes based on past experiences with population studies

a). In selecting groups for intervention studies care should be taken to avoid using as a basis a variable which will be influenced by the intervention. This is because of the natural shift toward the mean in both groups over time which will obscure any beneficial effect.

b). Intervention studies must control for all nutrition variables.

c). Dietary intake studies as currently odne, are very imperfect.

d). Clinical-biochemical indices to do with many micronutrients are quite good IF controlled for physiological variables, but indices to do with energy intakes and/or utilization are very imperfect.

e). Correlations between clinical-biochemical indices of nutritional status and measurements of nutient intake are poor for some nutrients.

f). Intervention studies in communities are generally less sensitive than controlled metabolic studies in demonstrating relationships between two or more clinical variables, particularly when cause and effect are the issue. However findings from controlled metabolic studies may be difficult to demonstrate in community studies because of the many uncontrolled variables which produce background noise. A failure to show a relationship in community studies does not imply that the relationship is untrue, or unimportant.

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TABLE 2

SOME EXAMPLES OF INDICES TO BE ASSESSED, ETC.

Ranges of Food Intake	Indices of Nutritional Status	Indices of Disease Vulnerability
(Given factors*, ranges of energy, nutrient intake for different age, body size, sex, illness categories) Surveys on food/nutrient Intake: (Availability Consumption), according to: age sex family structure and size social class community factors *Factors effecting absolute requirements and absorption-illness, Physiological state	Anthropometric eg. Skin-fold thickness Midarm circumference Wt-for-Ht Ht for age Hematologic eg. CBC Biochemical eg. Ferritin Al Albumin Transferrin Complement C_3 Iron Zinc Copper Folicin Vitamin A Vitamin C etc. Clinical assessment eg. Xerophthalmin Pluckable Hair Radiological eg. Bone age Metephyseal integrity etc. etc.	Cell-mediated immunity Skin tests T cell number* Humoral factors Opsonic function Antibody affinity Phagocyte function Intrecellular killing* Leukocyte mobilization responses Mucosal clearance of particles Epithelial cell-receptor function Etc., etc. *Requires more venous blood samples

As far as possible, all the indices should be accurately quantifiable.

TABLE 2 (CONTINUED)

Illness and Syndromes	Outcome	IMPACT
Infections eg. Pyrogenic parasitic viral mycobacterial etc. Deficiency disorders Diarrheal syndrome Ill-defined febrile illness Metabolic-toxic disorders Psycho-behavoiral Longevity Menarche Etc., etc.	-Decline in physical activity -Anorexia -Weight loss -Pemanent seq. -Impairment to mother's occupational competence -Impairment to male's occupational competence -Impairment to social competence —Impairment to financial status -Impairment to sensory function: Sight Hearing Taste	Morbidity-Health resource usage - # days out of: school work -Household mismangement: Adult Child disease Child care Adult/Child nutrition ⇓ Community Impact Loss in: -income maintenance and growth of income -social security -educational levels -Productivity -"Quality of Life"

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NUTRIENT INTAKE AND DISEASE RESPONSE

Areas for future research

R.K.Chandra

1. Evaluation of the adequacy of humoral, cell-mediated and secretory immune response to conventional immunization procedures and the effectiveness of vaccine-induced protective immunity.

   The choice of the infection to be studied depends upon the prevalence of the disease in the community. In many developing countries, measles would be an obvious choice. The study could look at the immune response to live attenuated and killed vaccines and correlate it with nutritional status assessed on a number of parameters. This would be followed by a careful study of the vaccinated group for the next 2-3 years, and noting the incidence of measles.

2. Is impaired immunocompetence in undernutrition a threshold phenomenon or does it alter progressively with increasing severity of deficiency ?

   This question needs to be answered for postnatal as well as intrauterine malnutrition. There is need for the assessment of immunity function of mildly and moderately undernourished children and adults and of infection-related morbidity and mortality. For some specific nutrient deficiencies, eg iron, altered immune response is a threshold phenomenon.

3. Definition of the role of maternal malnutrition in the pathogenesis of low birth weight and associated impaired immunocompetence.

   This may be achieved by epidemiologic correlative studies, and prophylactic or therapeutic intervention studies. The difficulties of the interpretation of the data available to date should be defined and appropriate corrections built into the proposed study. Eg matching of groups for antenatal care, maternal height, socioeconomic grade, family size, etc. A frequent drawback of many published reports is the lack of data on total nutrient intake of the mother, including that supplied as supplement. The many other determinants of birth weight (outlined in a recent WHO document MCH/LBW/78) should be taken into consideration. Also, indices of biological competence should be employed for assessment of the effects of nutritional supplementation, rather than birth weight alone.

4. Assessment of the nutritional and immunologic correlates of postoperative sepsis and infections among hospitalized patients

Such an evaluation would highlight the indices that point to a high-risk individual. This should be extended by studies on the incidence of infection and immunodeficiency in patients given deliberate nutritional supplements to correct metabolic balance.

5. Evaluation of the nutritional and immunologic status of old individuals and its correlation with the incidence of disease.

Epidemiologic correlative as well as intervention studies are required in this area.

6. Assessment of the nutritional and immunologic profile of patients with cancer and its correlation with incidence of infectious illness.

Prophylactic and therapeutic supplementation to bring these individuals into positive metabolic balance should be attempted and correlated with the occurrence and type of infections.

7. Complications of infectious diseases in relation to nutritional status.

There is a paucity of morbidity data in individuals with mild to moderate nutritional deficiencies. Also, subjects who have been immunized when they were undernourished may be at greater risk of developing immunopathologic complications of infections; eg severe Arthus phenomenon -like illness in malnourished children previously vaccinated with live attenuated measles virus and subsequently exposed to natural virus.

8. Incidence and severity and natural history of atopic disease in populations with rampant parasitic infestations and elevated IgE antibodies.

9. Evaluation of some aspects of immunity in undernutrition that have been inadequately studied or not studied at all.

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NUTRITION, MALNUTRITION, AND DISEASE:

A SOCIAL SCIENCE PERSPECTIVE

John Osgood Field

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

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 nontechnical, 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 read 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

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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

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-existant. 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.

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

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

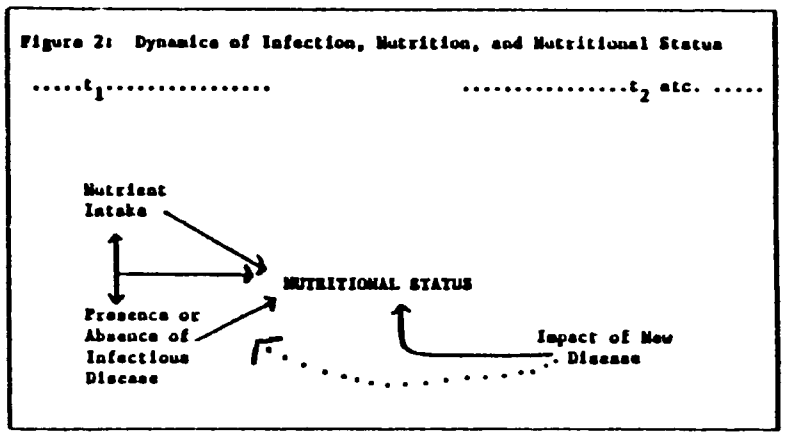
[2] Michael C. Latham, "Nutrition and Infection in National Development," in Philip H. Abelson, Food: Politics, Economics, Nutrition and Research (Washington, D.C.: American Association for the Advancement of Science, 1975), p. 69.

[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 Moisés Béhar, 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]

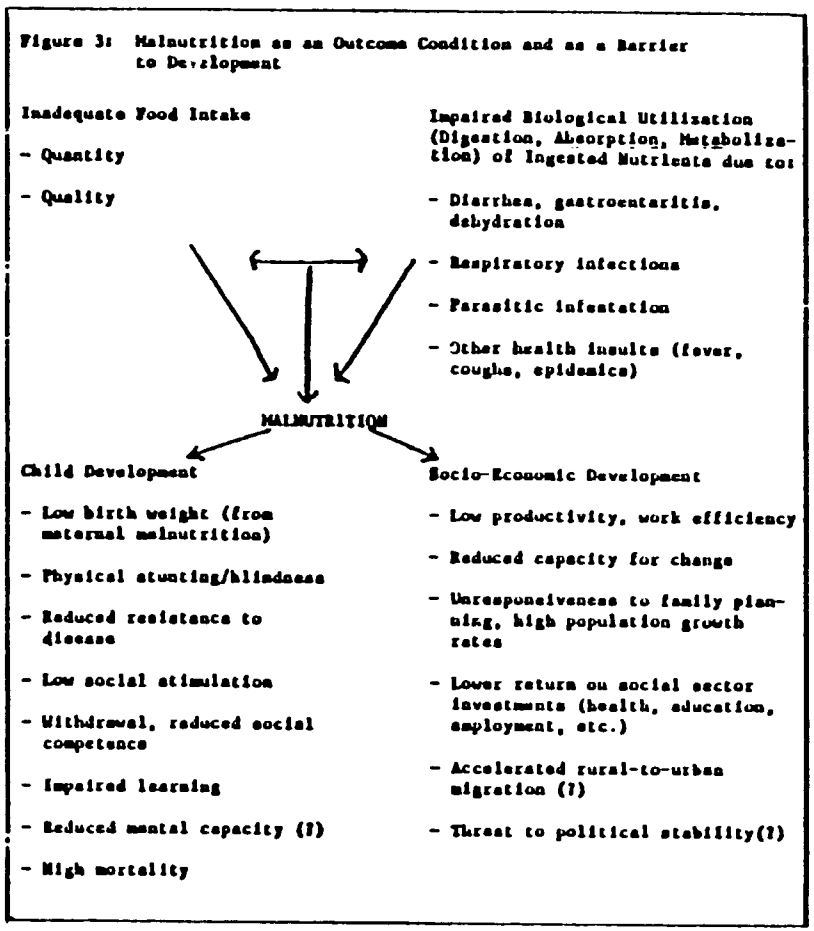
Research Focus #2: The Functional Effects of Malnutrition

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



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.[7] 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.

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.

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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 resistance - 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 Seghie 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 Seghie, "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 so 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

[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.

[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 H. 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

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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

[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 Annual; of Kerala," Hastings Center Report (February 1977), 34 - 42; and Cutchin, op. cit.

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care, 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

[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 affects 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]

[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

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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]

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[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 Joe Bobbs'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.

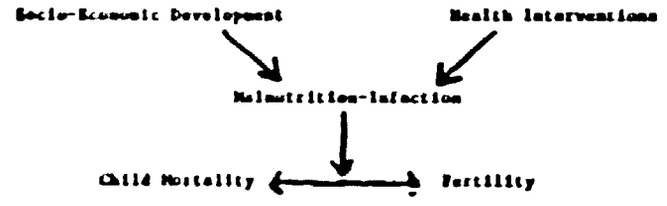
3. Health Dynamics

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 manner 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 3. 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 income, urbanization, literacy composition, 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 on the more, given an established pattern of overall development.[28]

[28] To illustrate, among the simple models shown in Figure 3 and a body of data which is by no means conceptual, the M I T-Cairo University Health Care Delivery Systems Project has unearthed a fascinating series of statistical relationships (some quite unexpected) which have helped Egypt's Ministry of Health to understand better some of the health dynamics particularly as such 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 analyze vaccinated births and childhood deaths. (These studies are currently in draft form and will soon be available in a formal version. 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 as well. Similar studies elsewhere might make equally useful contributions.

Figure 3: 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.

not 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 preventive, population based, and ancillary 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 Ishak Adisra and Paul Zahla, "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 Mahim 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.

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Nutrient Intake and Disease Response

R.K.Chandra

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.

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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, perticularly Ascaris, Necator americanus,

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Strongyloides 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 concurrent observations in a control group. Again, a Tanzanian study suggesting a lower infection rate in iron-deficient 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 impaired cell-mediated immunity has been extensively reported. Several types of evidences were collected: Cutaneous delayed hypersensitivity to a battery of multiple 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 efferent 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, [illegible]ure 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 rachallenge 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. Immunostimulation 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 preprogeancy, 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 AGING

There are several facets of interaction between nutrient intake and the process of aging. 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 infections 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, aging 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 necessitating 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.

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.

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 malabsorption 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 malabsorption 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 related out, however, that the ecosystem that breeds

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