PROGRAM DEVELOPMENT FOR INTERVENTIONS IN THE MALNUTRITION-INFECTION COMPLEX

Subcommittee on Interactions of Nutrition and Infection Committee on International Nutrition Programs

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NOTICE

The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the Councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the Committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

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SUMMARY

The magnitude of malnutrition in the world is staggering. In addition to its major causative factors, which relate specifically to food availability at the household level, infectious diseases are an omnipresent and important inciter and contributor to malnutrition and its associated morbidity and mortality. Therefore, there are many factors that deserve attention during any examination of the malnutrition-infection complex.

This report addresses only those factors expected to reduce the impact and burden of infectious diseases as a means to improving nutritional status and concentrates on recommendations for field-level implementation programs. To accomplish this, the subcommittee examined the following:

• the interaction of nutrition and infection, which is called the malnutrition-infection complex;

• targeting of programs to specific subsegments of the population, specifically to pregnant and lactating women, weanlings and children less than three years of age;

• incorporation of adaptive research and impact evaluation into the program design; and

• national planning and policymaking, local-level responsibility, outreach to the household level, and the establishment of linkages between the national and local activities.

The subcommittee recommends that four elements be included in the program as a "package":

• Prenatal control to increase maternal caloric intake through education and/or supplements (preferably using indigenous foods), however provided; to eradicate
to monitor weight gain by distributing take-home charts on which infant birth weight and growth can be recorded; and to initiate nutrition education, including concepts of breast-feeding, maternal requirements for lactation, weaning foods, oral rehydration therapy for dehydration, and postinfection convalescent nutritional care.

- Emphasis on promoting breast-feeding, prolonging the practice as long as possible, and introducing supplemental feeding practices with locally prepared indigenous foods. Completed growth charts and calculation of incremental growth will assist in the identification of growth-faltering infants, a group requiring extra attention.

- Introduction of oral rehydration into households and instruction in its proper use in early therapy for acute diarrhea, along with continuation or early reinstitution of feeding for nutritional maintenance.

- Programs to immunize children less than one-year-old with DPT (diphtheria-pertussis-tetanus), BCG (bacille Calmette Guerin), measles, and polio vaccines while the child is adequately nourished (as established by growth surveillance) and to maintain immunization records by means of growth charts that are completed in the home.

Because there should be no dichotomy between doing and learning, the subcommittee recommends that the program include a research arm that would seek the information necessary to shape and define efforts to achieve maximum efficiency and success.
I. GENERAL COMMENTS

The magnitude of the problem of malnutrition in the world is indicated by recent estimates that as many as one-half to one billion people suffer the consequences of inadequate nutrition (1). The three fundamental underlying causes of this malnutrition are poverty, unstable food supply, and failure of governments to develop nutrition policies. All of these are significantly modified by sociocultural factors that are specific to different populations and geographic regions.

This report will not deal with these larger issues, which go far beyond the scope of the subcommittee's charge. Rather, it contains recommendations of field-level programs that are designed to improve nutritional status by reducing infection in populations that suffer from malnutrition.

This position paper is based on proceedings of five workshops on malnutrition and infection (2-6). These workshops demonstrated that malnutrition and infection interact to the detriment of the host. The first (2) of these workshops documented the high prevalence of intestinal malabsorption in large numbers of individuals in developing countries, particularly as revealed by absorptive function tests using the sugar xylose. While this abnormality could not be translated into a quantitative effect on nutritional status, intestinal infections were implicated as one possible cause of asymptomatic malabsorption in these populations as well as a consistent cause of clinically significant malabsorption of multiple nutrients during, and, for a while, after acute infections. Some data suggested that the inverse relationship between infection rate and growth rate in young children was due in part to infection-induced malabsorption.
The second workshop showed that infection in pregnant women adversely affected birth weight of the fetus and that it correlated with poor growth and increased morbidity and mortality in infants. Thus, concern for the general health of the pregnant woman, including nutritional status and infectious disease morbidity, could be expected to improve the growth and health of her offspring.

In the third workshop, the impact of malnutrition on host defense mechanisms was thoroughly reviewed. Relevant studies showed a measurable negative impact on immune function, particularly on the complement system and cell-mediated immune mechanisms. The implications for immunization programs were reviewed and clearly showed the benefits, in terms of both safety (especially with live agent vaccines) and efficacy, of immunization before malnutrition develops.

The fourth workshop took a quantitative look at the nutrient losses and needs during infection. The detailed papers that were presented established that infection alters nutritional status in all patients. The ultimate impact depends on the nutritional state of the host at the time of infection and the host's ability to replete losses rapidly during early post-infection convalescence, when cumulative losses are maximum and the host is most vulnerable to repeated infections. Indeed, when nutritional repletion is not possible, which is manifested in children by failure to catch up in their growth, recurrent infections usually initiate a cyclic deterioration of nutritional status and health. Inexorably, this results in overt protein-calorie malnutrition, which is often fatal. There were two noteworthy conclusions from this workshop: there is a need to emphasize health care training and prophylaxis, especially to control acute diarrheal disease, and there is a need to maintain adequate intake of calories during and after infection.

In the fifth of these workshops, there were attempts to evaluate the roles of various interventions to reduce the burden of infection with direct and indirect nutritionally
oriented programs, as well as environmental and personal health interventions. These evaluations formed a part of the program recommendations that are discussed below.

Planning an effective intervention must take into consideration the multiplicity of interactions of infections and nutritional state, which the subcommittee calls the "malnutrition-infection complex." A number of possible actions can be taken now and can be expected to give immediate results. Other actions must be deferred, either because there is insufficient background information or because they would be too costly and of relatively limited benefit to be worth the effort. When resources are limited, priorities must be assigned for such actions. The process of assignment must take into account both feasibility and relative beneficial yield.

The important issues of malnutrition and infection justifiably dominated the deliberations of the workshop. However, the final desired goal—an energetic and productive society—must be considered in the recommendations proposed herein. Within this context, the young must receive priority attention, because they are most affected by the malnutrition-infection complex and will show the greatest response to intervention. Initially, the target subpopulation should be limited to three groups: pregnant and lactating women, weanlings, and young preschool children (especially those less than three years of age).

This is not to suggest that other segments of population, such as school children, the disabled, the elderly, and, in some areas, the working adults, do not deserve attention, but with limited available resources the target groups indicated above deserve priority consideration. The easiest way to reach these target groups—and some other groups as well—is through the household and its manager, the mother.

The approaches to the problem must include interventions directed against the malnutrition-infection complex. There is a considerable body of evidence indicating that infectious diseases exert a major and adverse impact on nutritional status.
This is clinically evident in individuals already malnourished, overtly or even marginally (5). Although there are many important research questions in the vast area of medicine, biology, physiology, and biochemistry that are compressed into stark simplicity by the above summary statement, the subcommittee has considered them here only as they may relate specifically to the development of programs to reduce consequences of malnutrition and the burden of human infectious diseases. Neither has the subcommittee systematically examined the large number of options or strategies available to achieve the stated goal. To a large extent this has already been done in June 1978 at a meeting organized by this subcommittee. The proceedings of this meeting, Successful Interventions to Reduce Infections in Malnourished Populations, will be published in the 1978 November-December issue of The American Journal of Clinical Nutrition (6).

The subcommittee proposes that four technical assistance programs be instituted throughout the world, that long-term funding be committed, and that sufficient resources be provided to incorporate programming concerns into policymaking early in the process, and in a continuing fashion. To a large extent these measures are preventive rather than curative. The programs must be designed so that suitable methodologies can be implemented in each country, region, and cultural milieu. They must also include provisions for training at all levels. Evaluation of progress is essential. Inasmuch as persons directly involved in the program might well have difficulty assessing their own performance, experts external to the program should participate in this process.

All of these applied programs must be geared to development of local competence and use of local resources. Recommendations contained in this report will not be directed toward population control. While this is clearly a major issue within any health program in the developing countries, population control is being addressed by other groups. However,
it is the opinion of this subcommittee that improvement of health and reduction in mortality of children will lead to a reduction of birth rate.

INTERDEPENDENCE OF ADAPTIVE RESEARCH AND IMPLEMENTATION

Central to our evaluation of program development is the premise that it is less important to determine the specific interventions than to establish an adaptive research orientation for their implementation. By this the subcommittee means that the most critical process is the attempt to answer the "how" questions -- how to implement, how to teach, how to motivate, and how to evaluate and adapt results for maximum gain -- rather than to ask what instrument is to be used. In this context, research cannot be separated from implementation. Information derived from the research (evaluation) component is used to adjust the performance of the intervention in a feedback loop uniting service and study.

It no longer seems reasonable to implement single intervention schemes in isolation. Just as there is growing recognition of the need for national nutrition planning efforts to accomplish nutritional goals, there is a growing recognition of the need for integrated planning of health interventions to attain specific health program goals. This is not to suggest that the subcommittee recommends an all-or-none approach to the package of interventions. There may well be circumstances under which one or two, but not all, of the programs can be initiated. This should, by all means, be done. Nevertheless, for maximum efficiency the process should include the full range of programs described above and also allow for continuous adjustments of the individual 'components through performance and impact feedback.

At the same time, there is also a need for a strong and responsive education component, which contains both a two-way
transfer of information and a sensitivity to cultural cues. These aspects of the education process have often received inadequate attention in program planning, apparently because of an erroneous assumption that culture-free information need flow only unidirectionally, from agent to recipient, from educated to uneducated, from those who have to those who have not.

The implementation of this concept of technical assistance would create a major contemporary revolution in intervention strategy. This challenge should be pursued first in the demonstration/training project in which biomedical and social scientists, policy and planning personnel, politicians, and field workers join efforts for a long-term effort that is designed to work out practical delivery tactics and second in the actual spread of indigenous programs that are designed to reach the targeted populations. The latter goal is of the greatest importance, for programs that look good in the planning stage will accomplish nothing if they fail to reach the people.

INFRASTRUCTURE

The four recommended program elements are home-based education/service modules, which remove even the classical medical interventions of rehydration therapy and immunization from the hospital physician or the rural health center. Effective programs must actively reach out into individual households rather than become "institutionalized." If the goal is to reduce the prevalence and severity of malnutrition, then health services must be ranked according to their impact on nutritional status. The catalytic response should improve both health and nutrition status. However, this will demand both an extraordinary degree of coordination of efforts and a reduction in the sectoral jealousies that often plague interventions.

First, a national strategy must be developed to improve the nutritional state of the population. This should be
within the purview of an agency or council with the power and the responsibility for national planning and policy-making and should involve the economic, agriculture, health, education, and welfare sectors. The lack of such planning is one of the basic contributors to malnutrition.

Second, major responsibility and action should be delegated to the recipient population, ideally through the mother in the household. In this way local resources and talent may be motivated and used as efficiently as possible. Simultaneously, the avoidance of dependency is assured.

The third requirement is a system that links the national and local administrative levels to provide for data collection, impact analysis, and responsive planning, as well as for training, procurement, and distribution of whatever special items are to be used or dispensed in the program. The mechanism to accomplish this will undoubtedly vary from country to country, depending on the system of power and political authority. Considerable insight, creative thought, and innovative methods will be needed to make the often cumbersome bureaucracy responsive.

The most useful programs will address all of these needs in an integrated fashion and will establish the interventions, not as special inputs, but rather as routinely available services. This, in turn, means that it is essential to stress the use of locally available or indigenous resources, including trained personnel; locally produced foods, drugs, or other materials; and local capital, wherever and to whatever extent possible. Foreigners, imported products, or outside assistance are best used as catalysts or as sources of nonrecurring expenses, e.g., the purchase of machines that are necessary to start a program. Whenever operating costs are provided or foreign commodities are used, a suggested phase-out of such
assistance should be indicated clearly. In many countries the resources are already in the community -- they need only to be organized and directed to the problem. Yet there will be places where, and circumstances under which, chase-out is not possible and long-term direct support will be required. This issue should also be confronted directly and expressed clearly in the program plan.
II. PROGRAMMATIC ELEMENTS

PRENATAL CONTROL

The enormous social and economic importance of women in the functioning of the family has largely been ignored in the planning process. Programs for nutritional improvement and better health must deal directly with the needs and goals of these women if they are to succeed. The sociology of women throughout the world is rapidly changing, while at the same time their biologic contributions remain central. These facts must be considered carefully when developing intervention plans. In many nations, it is a major goal of women to achieve economic equality and social independence through work. Any campaign to promote breast-feeding of infants should recognize the primacy and the strength of the social goals and provide the necessary support to achieve them. Otherwise, it will be doomed to underachievement.

The overall program strategy should begin with the woman and then develop a system of support around her for specific interventions. Beginning with the pregnant woman, attention should be directed toward the developing fetus. In so doing, the philosophical approach must be to prevent malnutrition and infection rather than to find and treat it after the fact. Pregnant women are easily identifiable, but not always as easily reached. To meet the need for outreach, the subcommittee proposes that field surveillance be initiated to identify the pregnant women in the community in order to accomplish five objectives: 1) to increase their intake of calories by supplementing their diets with indigenous foods, by instructing them how to effect this themselves, or both; 2) to immunize them against tetanus with a single dose adjuvant-toxoid vaccine; 3) to treat them for nutritional anemia and other specific deficiencies (such as vitamin A, iron, and iodine); 4) to monitor their weight gain and to give them
take-home charts on which they can record both maternal and subsequent infant data, such as birth weight; and 5) to provide them with nutrition education to assure better infant care, including concepts of breast-feeding and weaning foods, oral glucose-electrolyte fluid replacement for acute diarrhea, acute and convalescent nutritional needs in infection, and maternal food requirements for lactation. At the same time, severely malnourished or otherwise ill women can be identified and referred for treatment. These tasks can be performed by nonprofessional trained field workers who are well supported and supervised.

The specific goals of this program are to improve maternal nutrition before and after delivery, to improve birth weight, to eradicate tetanus neonatorum, and to initiate a system of support and education of the mother to improve infant nutrition during the critical preschool years. The take-home records and the early initiation of education are an essential part of this process.

BREAST-FEEDING AND WEANING
At last, much attention is being given to the decline in incidence and duration of breast-feeding in many developing countries. Breast milk is recognized as a nutritionally ideal, universally available first food. But in addition to its nutritive qualities, breast milk enhances neonatal resistance to infection and promotes a protective intestinal flora to resist enteric pathogens. In the process, subtle psychological bonding phenomena between mother and infant develop, leading to a sensitive and durable interaction thereafter. Lactational amenorrhea is a positive force for increased birth spacing. Because of these factors, breast-feeding has been called "the main promotor of infant health" (7).
Four components are probably necessary for such a program to succeed: intensive efforts must be made to reeducate physicians on the critical importance of breast-feeding, because their opinions are influential and many of them favor formula feeding either directly or indirectly; labor policies must be developed to provide for maternal leave-of-absence and facilities for on-the-job breast-feeding by working mothers; advertising and promotion of multinational and local manufacturers of infant formula should be judiciously restricted; and mass media should be used to promote breast-feeding and to provide positive reinforcement in all socioeconomic classes of society. These components are possible within a firmly supported, integrated plan of action; whereas isolated components, subjected to intense counterpressures, would be likely to fail.

Those selecting educational efforts must avail themselves of all opportunities including national mass media campaigns, health professionals, and, most importantly, the outreach workers who will walk the campaign into each household. Because these several promotions will be mutually supportive, the resulting network should be strong and effective.

Although the ideal duration of exclusive breast-feeding is still controversial, ample evidence indicates that infants require nutritional supplements beyond 3 or 4 months of age. However, the safety and availability of breast milk as a continuing high quality food source dictates that breast-feeding be continued as long as the mother is able to lactate successfully, even until the infant reaches 24 months of age. During this time supplementary feeding should be increased to meet the needs of the growing child.

The "weaning" foods should be derived from indigenous sources, be nutritionally balanced, and be administered safely
and hygienically. The widespread use of imported or even locally produced commercial food products is not the best way to meet these needs in low income populations. Information and education for good weaning practices can be built into a system that engages the pregnant woman in an educational/service/surveillance network, which continues after delivery. Institution-centered mass feeding programs are not strongly recommended either. Instead, the emphasis should be placed on feeding in the home with home-produced supplements. Wherever required, the provision of supplementary foods must be targeted, not generalized. Through monitoring of infant growth, individuals showing progressive failure of incremental growth can be selected for nutritional supplementation. Whether this supplement should be provided in the home or at a central location where education, immunization, and specific diagnosis can also be achieved is a matter for future study.

ORAL REHYDRATION FOR ACUTE DIARRHEAL DISEASE

Morbidity and mortality that are attributed to diarrheal disease are caused by acute extracellular volume dehydration, cessation of caloric intake due to anorexia and cultural factors, and the catabolic response of acute infection. Oral fluid therapy is well suited to rehydrate the dehydrated patient, to maintain adequate volume during progressive diarrheal fluid losses, and to permit continued intake of calories during convalescence. Problems are centered on the practical introduction and application of oral therapy in different cultures throughout the world.

Simple glucose and electrolyte fluids given by mouth save lives when administered to victims of severe diarrhea. The vast majority of mild to moderate diarrheal patients can be successfully rehydrated and maintained with oral fluid alone. By preventing or reversing acidosis and counteracting vomiting, oral rehydration permits continued feeding, including breast-feeding, thereby maintaining more normal caloric input. Although continued breast-feeding may increase the volume of diarrhea, an increase in oral glucose-electrolyte fluid therapy safely maintains fluid balance. The combination of oral therapy and
continued feeding of children with repeated episodes of diarrhea maintains their nutritional status (8). By permitting more rapid restoration of nutrition and "catch up" growth, oral rehydration plus feeding helps to prepare the child to resist and respond as well as possible to the next infection, which will inevitably occur.

While the technology, safety, and efficacy of oral therapy are well established, the acceptance of the techniques and their delivery to each diarrhea patient in many cultures is not known. Questions of who can deliver oral therapy and how it should be delivered cannot be answered by a single study, but must be investigated for each culture and adapted to local practices and beliefs. Most villages will have many cases of diarrhea each week of the year; however, few cases will be reported to a local health facility because of distance, cost, and cultural barriers. It is also not reasonable to expect that mobile family-health workers will visit each household with diarrhea. Most episodes are, and will be, treated at home by the mother.

In the program to implement oral rehydration the mother must be instructed how to assume new importance in her role as dispenser of care. Successful oral therapy will depend upon educating the mother to mix and administer properly a glucose (or sucrose) electrolyte solution and to continue the provision of a normal caloric intake.

In some regions and in hospitals and dispensaries it may be economical to dispense the powdered glucose and electrolytes in a prepackaged form which is easily added to a standard volume of boiled water just prior to use. However, marketing and cost barriers to universal distribution of oral therapy packets make it desirable to explore methods of mixing and using sucrose and salt, which are available in local markets. The solubility and purity of the salt and sucrose that are sold in these markets should be examined and methods of measurement, such as bottles and spoons, should be designed or standardized. The instructions and teaching techniques for proper mixing of ingredients should be tested to assure that correct concentrations of sucrose and electrolytes
are delivered to the diarrheic children. The mothers must also be given simple instructions on how to determine if a child can be treated at home, if a health worker should be called, or if the child should be taken to a local health facility. The "when-to-refer" decision will obviously depend on the severity of the diarrhea and the accessibility of health professionals and facilities.

Education of the mother and health professionals on the use and efficacy of oral fluid will encounter barriers that commonly accompany the introduction of any new technology, regardless of its simplicity. The essence of this program will be to surmount these barriers. In some instances, recognized barriers can be overcome during the education process. For example, if diarrhea is viewed as a helpful process of "purging toxins", then oral therapy may be introduced as "assisting in the purging process while replacing the purged liquid with clean liquid." If local medicaments already exist for the treatment of diarrhea, they could be investigated for possible adaptation to the glucose/sucrose and electrolyte concentrations which are known to be most efficacious. Simple instructions on the administration of oral fluid, such as "one glass for every loose motion", must be devised and tested for comprehension by the mother and for safety, especially in the malnourished child. Mothers must be taught the necessity of continued feeding, especially breast-feeding, throughout the episode of diarrhea. Any concomitant increase in the volume of diarrhea must be matched with an appropriate increase in oral fluid therapy. Cultural taboos advocating the withdrawal of food during episodes of diarrhea must be countered by providing examples of uninterrupted feeding that have produced successful recoveries.
IMMUNIZATION

The provision of vaccines for prophylactic immunity is more readily seen as a preventive approach to infection in the malnourished than are prenatal control, breast-feeding, weaning supplements, or oral rehydration for acute diarrhea. However, linkages among these various elements and immunization have already been established. For example, immunization of the pregnant woman can prevent neonatal tetanus. In the future, there may also be techniques to enlarge the complement of protective antibodies in breast milk to protect suckling infants. Maintenance of good infant growth will ensure the best immune response to vaccines, while the home-based record will provide the logistical tool to ensure maximum coverage of the population at risk.

The logical choice of vaccines will vary according to the agent or vector, cost, and the availability of new or improved products. Notwithstanding, within the first year of life most infants should receive DPT, BCG, measles, and polio vaccines. It may be necessary to develop a "cold chain" for transport and storage to preclude inactivation of temperature-sensitive strains. Households will have to be asked to maintain records of immunizations and a more effective system for extending maternal and infant care into each household must be developed.
III. FUTURE RESEARCH PRIORITIES IN SUPPORT OF PROGRAM EVALUATION

Concern for implementation of interventions does not remove the need to pose research questions. Programs should be shaped and sharpened to fit the needs of the community, otherwise poor cost-benefit outputs and failure to reach realistic goals will result. The subcommittee believes that the following four components should be incorporated into the program design in order to obtain the information necessary for informed decisionmaking.

**Prenatal Control**
How much food supplementation of the pregnant women is actually necessary to obtain a measurable benefit? There is a definite requirement for specific guidance on how much, what, and when. Simple outcome indicators are also needed. Can maternal weight gain be used to predict birth weight, neonatal mortality, or postnatal growth?

**Breast-Feeding and Weaning Foods**
What are the major factors, both general and local, that continue to contribute to the decline in breast-feeding in developing countries? What are the most important socio-political and educational techniques that are needed to reverse this adverse trend? What are the most effective means of augmenting the anti-infectious properties of breast milk and of prolonging production of sufficient quantities of high quality milk?

We need a better understanding and definition of normal growth. The Gomez classification, most readily implemented in the field, may be useful as an index of malnutrition during the first 12 to 18 months of life, but thereafter it reflects
past rather than present nutritional stress. To remove past events from consideration, weight in relation to height (more difficult to obtain because of field problems with measurement of height) or incremental growth (requiring a simple calculation) should be substituted. However, growth-faltering must be defined so that the child at greatest risk of infectious and malnutrition morbidity can be identified. What are the specific major external factors that produce growth-faltering at different ages in different cultures and climates?

It is essential to determine which local foods can be processed in the home to provide a nutritious and safe supplement to weanlings. An essential component of this effort is the evaluation of the educational process and the impact of agricultural policies that affect availability and pricing of the desired foods.

Oral Rehydration
Clinical trials are still needed to establish the safety of sucrose-electrolyte solutions in infants and severely malnourished children, and to determine the allowable errors in electrolyte solutions mixed in the home so that hypo- or hypernatremia can be avoided. Efficacy of oral rehydration in rotavirus infection has yet to be demonstrated, but studies to determine this are in progress.

Immunization
Two levels of research promise to improve immunization practices. Clinical investigation can solve immediate questions concerning the combination and timing of recommended immunizations -- BCG, DEPT, measles, and polio -- and the safety and efficacy of these immunizations in the severely malnourished child. The goal should be to provide the strongest immunologic
punch in the smallest shot thereby reducing the number of boosters and protecting children early in life.

The second level involves more innovative research whose goals would be to extend protection to infections currently not covered, especially the respiratory and enteric diseases. However, surveillance data must be obtained first in order to determine the prevalence of recently identified viral agents and the well-recognized bacterial pathogens in each geographic region. A vaccine for rotavirus awaits development of in vitro culture techniques for the antigen preparation. The efficacy of oral polio, the meningococcal, and polyvalent pneumococcal vaccines in children under 2 year of age and in malnourished children must be studied. The demonstration of cross protection between certain bacteria and between enterotoxins offers possibilities for common-antigen immunization. In addition, research on the molecular pathogenesis of these various infections offers promise of developing prophylactic measures not involving vaccines. Such research should elucidate the nature and specificity of surface membrane receptors, which determine many aspects of the host-parasite relationship.
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