NUTRITION AND PARASITISM

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INTRODUCTION

The possibility of contact between parasite and host is regulated by ecological and behavioral factors, but once contact is made, the outcome of infection is governed by factors arising from the innate and acquired characteristics of the host.
D. Wakelin

Dr. Wakelin's comment [1] is incisive in its characterization of the evolution of parasitic disease. The term "innate" characteristics referes to the genetic constitution of the host. To a nutritionist like myself, "acquired" characteristics immediately brought to mind dietary intake and nutritional status of the host. It is estimated that over one billion people are infected with the common roundworm, *Ascaris lumbricoides* [2]. An even greater number of individuals, perhaps a quarter of the world's population, is infected with hookworm [3]. The incidence of malaria is approximately 100 million cases per year resulting in nearly one million deaths, mostly in children under 14 years of age [4].

A consideration of the present topic is also important by virtue of years of neglect by research scientists. Keusch [5] has commented:

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> "Although an enormous proportion of the world's population is infected by parasitic agents (frecuently by several at the same time), parasitic diseases have often been left out of the picture in favor of the acute bacterial and viral diarrheas and respiratory disease. Quantitative data that demonstrate the importance of these latter diseases in the malnutrition-infection complex have been obtained, and programs of intervention have been developed. However, a similar formulation for the various parasitic diesease has not been undertaken, even though modern chemotherapeutic agents offer the possibility of successful mass control for some infections (those caused by *Ascaris lumbricoides*, for example), and insecticides can be effectively used for others (malaria), . . . , primarily quantitative data linking parasites and nutrition are lacking. In such a vacuum, governmental decisions may be made on *a priori* grounds and valuable resources wasted on ill-conceived or low-priority programs."

Finally, this topic appears to be a fruitful focus for the discussion of several important biological issues that highlight the workings of genetic factors in the expression of human disease.

Taxonomy of Parasites

Prior to our discussing issues of interaction, however, it is important to provide a brief orientation to the classification to the classification of human parasites. A parasite can be defined as an "organism that lives on or in another and draws its nourishment therefrom." [6]. They can be classified first by their location, as *ectoparasites* or *endoparasites*. Ectoparasites live in the integumentary regions of the body, e.g. mites, lice, ticks, and affliction with these organisms is termed *infestation*. Endoparasites are found on mucosal surfaces or within the body itself, e.g. malarial organisms, intestinal protozoa, and cause *infection*. Our discussion will be confined to a consideration of endoparasites.

Endoparasites can be further subdived taxonomically into two sub-kingdoms within the animal kingdom: the unicellular organisms or *protozoa;* and the multicellular organisms or *metazoa*. These are further subdivided into phyla, classes and finally into individual species. Examples are listed in Table I [7]. A comprehensive listing of metazoan endoparasites (worms) with proven or suspected pathogenicity has been compiled recently by Mata [8]; it included 72 different species.

Finally, on a biological basis related to the location of the infection within the host, parasites can be classified as visceral or *blood-borne* (those that circulate in the bloodstream or take up primary residence in deep internal organs) and *intestinal* (those that live in the alimentary tract or in the mesenteric circulation). Malaria, Changa' s disease, onchoceriasis, and African sleeping sickness are parasitoses caused by blood-borne parasites while amebiasis, giardiasis, schistosomiasis (mansoni) and hookworm disease are intestinal parasitoses [7].

TABLE I Classification of Pathogens

Subkingdom	*Phylum*	*Class*	*Representative genera*
PROTOZOA (Unicellular)	*Protozoa*	*Sarcodina (amebas)*	*Entameba*
		Mastigophora (flagellates)	*Trichomonis*
			Giardia
			Leishmania
		Ciliata (ciliates)	*Balantidium*
		Sporozoa (Sporozoans)	*Plasmodium*
			Toxoplasma
METAZOA (Multicellular)	*Platyhelminthes (flatworms)*	*Trematoda (flukes)*	*Fasciolopsis*
			Schistosoma
		Cestoidea (tapeworms)	*Diphyllobothrium*
			Taenia
	Nemathelminthes (roundworms)	*Nematoda (roundworms)*	*Ancylostoma*
			Ascaris
			Strongyloides
			Onchocerca

The Two-Dimensional Nature of the Interaction of Nutrition and Parasitism with Genetic Factors

The present topic provides us with a potentially more *dynamic* exploration of the exercise of genetic factors in human biology because of the inherently two-dimensional nature of the concepts under discussion. This is illustrated schematically in Figure 1. It emphasizes fundamental assumption in genetics that neither nutrition nor parasitism can influence the gene (at least in any given generation). Genetic variation can, however, affect the demand for and/or the utilization of nutrients. Genetic variation can also affect the course of an exposure to parasites.

Examples for limb A of our scheme (Fig. 1) have been discussed eloquently elsewhere in this Workshop. Dr. Jackson discussed evidence for a change in the utilization of glycine in sickle cell anemia while Prof. Rosenberg describes the mechanism for increased demand for vitamin B_{12} in certain forms of methylmalonicaciduria. These are both examples with clearly defined genetic markers. The discussion of individual variation in nitrogen metabolism by Profs. Scrimshaw, Payne and Beaton suggest that genetic factors might also be operative in defining protein requirements; as yet, however, no genetic markers have been defined.

Some classical illustrations of limb B of our scheme - genetic influence on parasite: host interaction - have been described with respect to malaria. Most

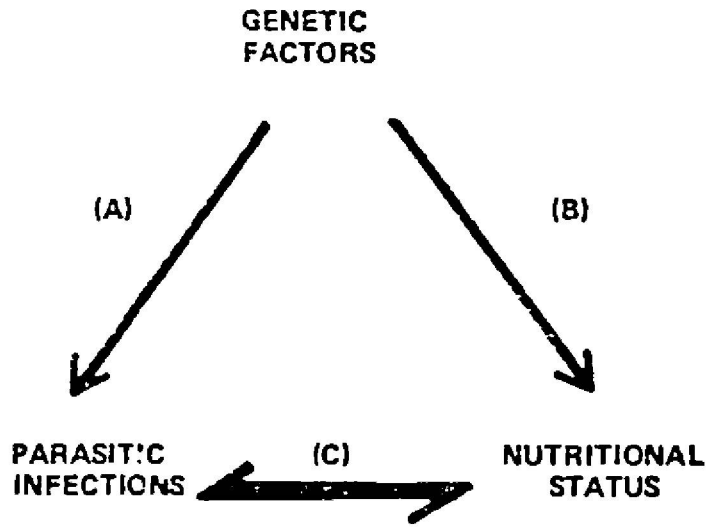

Figure 1. Schematic representation of interactions among genetic factors, parasitic infection an nutritional status. Genetic influences affect both susceptibility to parasitic infection and the nutr tional status. Parasitoses and nutritional status have reciprocal interactions of both synergistic an antagonistic natures. Beisel [18] with permission of the copyright holder. The University of Chicag Press.

famous, perhaps, was the demonstration by Allison [9] that individuals heterozy gous for the sickle hemoglobin gene (sickle trait) had lower levels of parasitemia with one form of malaria organism, *Plasmodium falciparum*. This protection did not extend to *P. malariae* infections. The classical molecular explanations for this phenomenon relate to the *in vitro* demonstration of lower invasion rates, the reduced intraerythrocytic multiplications, and the increased sickling of red cells with SA hemoglobin, all under conditions of low oxygen tension analogous to the venous beds of the human circulation where *in vivo* replication of plasmodia usually proceeds [10]. Epidemiological observation of a higher gene frequency of two other inherited human hemolytic diseases -glucose-6-phosphate dehydrogenase and thalassemia - in areas originally endemic for *P. falciparum* malaria led to the speculation that these disorders might also provide protection against parasitemia [11]; the evidence, however, is less conclusive [12].

Another example for limb B of the scheme is the documentation in Dr. Louis Miller's laboratory that the Duffy blood group (FyFy) determinants govern susceptibility to invasion of human red cells by the simian malarial parasite, *P. knowlesi*. The erythrocytes of individuals who are Duffy group-negative are resistant to invasion [13]. A similar finding was seen with the human pathogen, *P. vivax.*, in Duffy-negative individuals [14]. Since most black Africans are Duffy negative, a natural resistance to *P. vivax* due to this genetic factor operates to the advantage of the indigenous populations [15].

The most intriguing aspect of the scheme illustrated in Figure 1, however, is the interaction between nutrition and parasitism (limb C). Nutritional status can influence the susceptibility to parasitoses, and parasitic infection can affect nutritional status. Since, as discussed, genetic factors can influence both parasitic

infection and host nutriture, the bidirectional nature of the interaction between the latter two conditions sets stage for a truly two-dimensional character for the total interaction. This two directional interaction of nutrition and parasitism is discussed in detail in the subsequent section.

Synergism and Antagonism in the Interaction of Nutrition and Infection

An important concept in the biology of communicable (infectious) diseases was developed in 1959 by Scrimshaw, Taylor and Gordon in a paper entitled "Interactions of nutrition and infection" [16]. This was later expanded and embellished in a WHO Monograph 9 years thereafter [17]. In these treatises, they compiled the available evidence from animal experiments and observations in human studies, and expounded a principle which, simply stated, dictated that malnutrition and exposure to pathogens often *interact* in a given host such that the simultaneous effect of both conditions together is not equivalent to the sum of the effects of each occurring separately (Table II). This interaction could be *synergistic,* such that malnutrition increased the susceptibility to and/or the disease burden of a given infection, or, conversely, infection causes a deterioration in nutritional status; alternatively, the interaction could be *antagonistic,* such malnutrition decreased the susceptibilite to and/or morbidity from a pathogenic organism (see footnote in Table II). Examples of each of the potential reactions are illustrated in Table II. Concepts of synergism and antagonism have been discussed recently in detail, specifically for parasitic diseases and malnutrition, by Beisel [18].

Parasitic Infections on Nutritional Status

Synergism: Falciparum malaria in childhood produces growth retardation and stunting [19-21]. Parasites that produce intestinal bleeding, e.g. amebas, hookworm, can obviously impair iron nutriture [22, 23]. *Diphyllobothrium latum,* the fish tapeworm, competes with the host for intraluminal vitamin B_{12}; frank vitamin B_{12} deficiency with anemia and neurological degeneration have been observed [24, 25].

Nutritional Status on Parasitic Infections

Synergism: Protein-energy malnutrition (PEM) seems to aggravate infection with certain parasites. Studies in severely malnourished, hospitalized children in Costa Rica by Lopez et al. [26] showed a high rate of colonization with *G. lamblia.* Malnutrition reduces gastric acid secretion, and in the Costa Rican study, giardial prevalence was directly correlated with achlorhydria. Observations both in South African children with kwashiorkor and in North American children with hematological malignancies, suggest that PEM conditions the expression of *Pneumocystis carinii* pneumonia [27].

TABLE II

EXAMPLES OF SYNERGISM AND ANTAGONISM IN THE INTERACTION OF NUTRITION AND PARASITIC INFECTION

SYNERGISTIC INTERACTION AND ANTAGONISTIC INTERACTION	
PARASITIC INFECTION ON NUTRITIONAL STATE	*NUTRITIONAL STATE ON PARASITIC INFECTION*
SYNERGISTIC INTERACTION	
Malaria on growth	*Protein-energy malnutrition on giardiasis*
Amebiasis on iron status	
Hookworm	*Protein-energy malnutrition on pneumocystosis*
Diphyllobothrium latum infection on vitamin B_{12}	*Protein deficiency on schistosomiasis*
	Calorie deficiency
ANTAGONISTIC INTERACTION	
	Iron deficiency on malaria parasitemia
	Vitamin E deficiency on rodent malaria
(see footnote)	*Protein-energy malnutrition on schistosomal granulomata*

Note: In an experimental mouse model of schistosomiasis, severe caloric restriction ameliorated the hypoalbuminemia (ref. 29), but it is unclear whether this is a nutritional phenomenon or a change in intravascular fluid distribution.

Severe protein deficiency as severe energy restriction in an experimental animal (mouse) model causes excessive morbidity and tissue changes, as compared to controls, after a challenge with *S. mansoni* [28, 29].

Antagonism: Of the 474 studies of nutrient deficiency involving all types of pathogenic microorganisms reviewed by Scrimshaw et al [17], 93 [20%] showed antagonism; i.e. a *less* severe infection in the presence of malnutrition. Beisel [18] has emphasized instances of this form of interaction with parasitic organisms. Examples in human subjects are rare. Murray et al. [30] treated iron-deficient Somalian refugees with therapeutic dosages of iron; malaria parasitemia appeared rapidly in some members of the iron-treatment cohort. Vitamin E deficiency has been found to confer protection against *Plasmodium berghei* infection in a rodent model of malaria [31, 32]. The decreased survival of the parasitized vitamin E-deficient red cells apparently retards the development of parasitemia; this may represent the acquired, nutritional analogue of the inborn, hemolytic disorders discussed aboye. Its relevance to human malaria has yet to be demonstrated, however. Finally, also from rodent models, has come evidence that PEM will reduce the development of granulomas in experimental *S. mansoni* infection [28, 29]. Since the inflammatory granuloma response is the pathogenetic basis of illness in schistosomiasis, malnutrition may contribute to less severe manifestations of infection. Once again, conclusive evidence for the operation of antagonism in humans remains to be developed [33].

Mechanistic Considerations

There are large gaps in our understanding of the interaction of parasitism and nutrition, but certain facts and speculations about the biological mechanisms involved are worth considering. That parasitic infection of the intestine can cause deterioration in nutritional status is not difficult to understand given the central role of the alimentary tract in the uptake of nutrients from the diet. The mechanism of nutritional impairment in gastrointestinal parasitoses are listed in Table III. Of note is the fact that nutrients can be lost in significant quantities through the intestine, and that febrile complications can cause catabolic losses. It has been claimed that giardiasis produces some of its antinutritional effects by favoring upper intestinal colonization by fecal bacteria [34].

TABLE III Mechanisms of Nutritional Impairment in Gastrointestinal Parasitoses

Impairment of enzymatic digestion
Impairment of mucosal absorption
Competition for host's nutrients
Gastrointestinal loss of nutrients
Catabolic loss of nutrients
Conditioning of bacterial overgrowth (?)

The facts that many types of nutritional deficits impair the functioning of t host immune defenses, and that parasites themselves can influence the immun logical processes of the host are believed to be instrumental in the mediation both synergistic and antagonistic interactions. The interrelationships are illustrat in Figure 2. Wakelin [1] has dissected various processes in the mammalian an parasite immune response (Figure 3). It becomes obvious that the same proces are also sensitive to alteration by nutritional factors. Moreover, as pointed out Keusch [35], in the host: parasite interaction, the parasite often uses disguise outwit the host's immune defenses. Secondary to either nutritional or genetic fa tors, however, the host may unwittingly retaliate. If the characteristics of intestir mucus are instrumental in the establishment of amebic infection in the colon, th genetic changes or nutritional factors that alter the composition of mucus, m reduce the susceptibility of the host to invasion.

The infectivity of *Leishmania donovani* in a mouse model seems to be link to a specific genetic locus mapped to chromsome 1 [36]. If the protein alterati which dictates resistance or susceptibility represents a cellular receptor site f the protozoa, then a mechanism by which both genetic factors and nutritior deficiencies could determine the virulence of *L. donovani* in the host could conceived of. Investigations to determine whether or not an analagous situati obtains with human leishmaniasis are currently underway.

Models for the Genetic Modulation of the Parasite: Nutrition Interaction in Humans

The purpose of the foregoing background biology was to set the stage f the understanding of the two-dimensional interaction with genetic factors p vided under our topic. Let us now explore some hypothetical, but plausib cases of interaction between parasitic infections and nutrition.

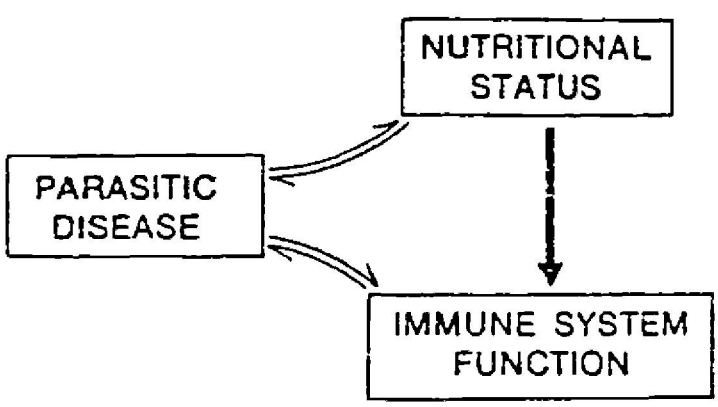

Figure 2. A schematic representation of the factors that cause synergistic or antagonistic chai in the serverity of parasitic diseases. Malnutrition in its various forms typically interferes functions of the immune system, while the nutritional status and immune system competenc the host have reciprocal influences on parasitic disease [18]. Reproduced with permission.

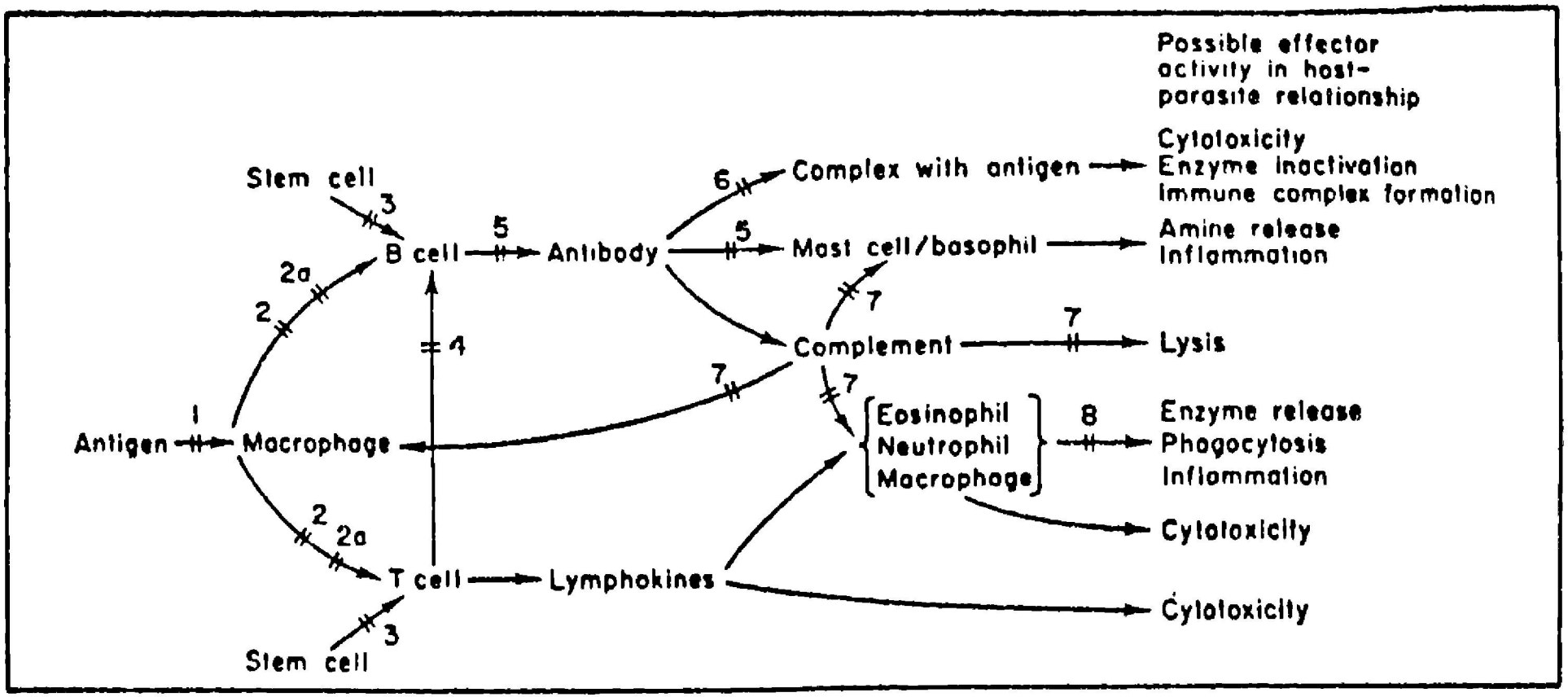

Figure 3. Diagram showing points at which genetic control may be exerted during the development and expression of anti-parasite immune responses. 1) Antigen handling by macrophage; 2) antigen presentation by macrophage; 2a) antigen recognition by lymphocyte; 3) stem cell deficiency; 4) T-B cell interaction (helper/suppresor function); 5) control of antibody production (class/level/specificity); 6) antibody affinity; 7) defects in complement components affecting lysis, chemotaxis, opsonization; 8) defective population or activity [1]. Reproduced with permission.

CASE # 1: Hookworm disease and iron nutrition

The first involves hookworm infection and iron nutrition. We know that there is variation in the population with respect to iron requirements; we shall assume that this is dictated primarily by genetic factors. If a fixed stress is superimposed uniformly on the population in the form of a constant hookworm infection of moderate proportions in all subjects, then the factor determining whether there be overt expression of deficiency manifestations or accomodation with complete preservation of iron-dependent physiological functions could be high intrinsic iron requirements (former) and low intrinsic iron requirements (latter). (Figure 4).

Another scenario involving the same parasite and nutrient could also be envisioned. In this case, a free-living population is assessed in a survey fashion using the determination of iron turnover as the index of individual iron requirements, and a distribution of individuals along a continuum of requirements is established (Figure 5). If, in fact, certain portion of that population had graded infections with hookworm, the differential worm loads, themselves, could have been responsible for the apparent (observed) distribution of iron requirements. If then mass chemotherapy were applied to this population and the hookworm eradicated, a subsequent survey might reveal a narrower

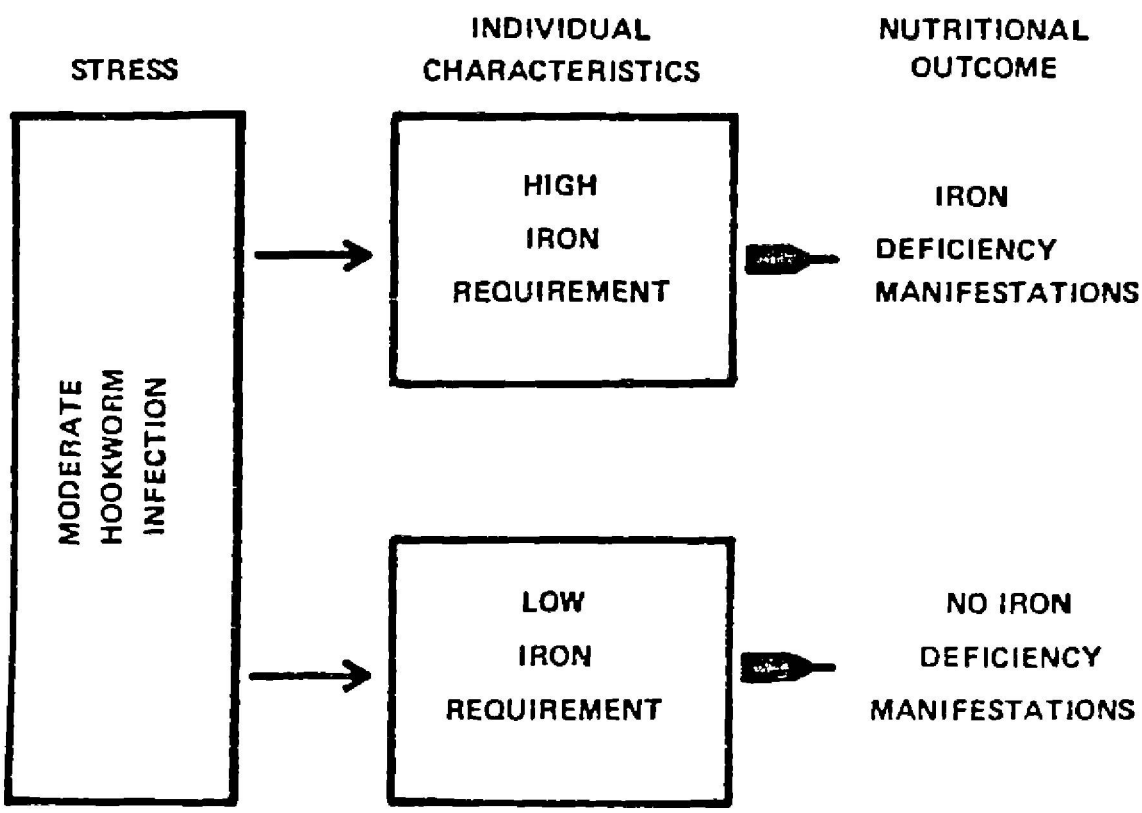

Figure 4. Schematic representation of the potentially differential nutritional outcome from a moderate hookworm infection. Individuals with high intrinsic (genetic) iron requirements would be more likely to manifest anemia than individuals with low intrinsic (genetic) iron requirements.

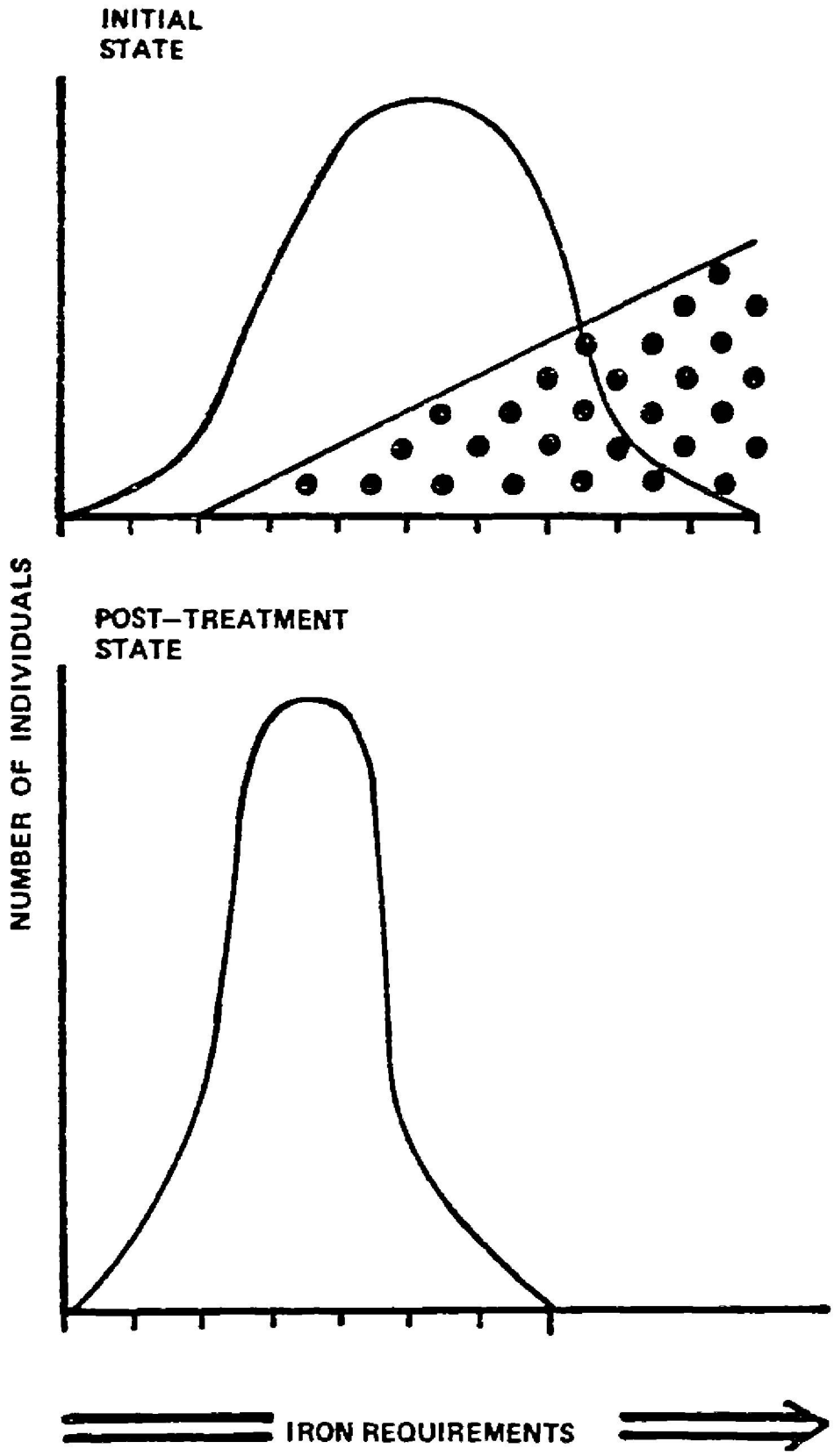

Figure 5. Hypothetical situation in which the distribution of iron requirements of a population was determined (initial state) without cognizance of a graded level of hookworm infection ranging from none to severe (dotter area). The distribution was again determined after chemotherapeutic eradication of hookworm infection in the population (post-treatment state). The distribution would be narrowed and shifted to the left. The individual ranking within the population might have changed as well.

range of variation in iron requirements and the individual ranking along th distribution might be substantially realigned (Figure 5).

CASE #2: Amebiasis and iron nutrition

Even more complex consequences of the interplay among genetic factors parasitism and nutrition can be envisioned. For a second case, let us conside special issues involving iron status and infection with *Entamoeba histolytic* (amebiasis). It has been observed that individuals vary in their resistance to th clinical evolution of symptomatic amebiasis after exposure to *E. histolytica* we shall assume that this represents genetic variation in host: parasite interac tion along the lines discussed by Wakelin [1], although the details are not ye understood.

A curious biological aspect of the ameba has been recognized: its remarkabl requirement for iron [37]. This has been explored in a golden hamster model in th laboratory of Dr. Louis Diamond [38]. These workers demonstrated a greater sus ceptibility to severe hepatic lesions in hamsters overloaded with iron that wer challenged with cultured amebae. Elsdon-Dew [39, 40] in Durban, South Africa had suggested that diet might play a role in the differential expression of amebiasi in local citizens whereby the European whites rarely had amebic dysentery or an other form of infection whereas in the black population (Zulus) fulminating ame bic dysentery and severe extraintestinal infection were common. Reanalyzing th South African experience, Diamond et al. [38] have suggested that iron overloa (nutritional siderosis) from consuming the iron-rich native (kaffir) beer migh explain the excess morbidity and mortality from amebiasis among the Zulus o Durban. Murray et al. [41] lend additional support to the association in controlled, prospective iron-supplementation trial among the Masai of Kenya They reported a greater prevalence of seropositivity and of stools positive for ame bic cysts and trophozoites in iron-treated subjects as compared to untreate controls. Thus, total-body iron status will be assumed to represent a nutritiona factor influencing the resistance to amebic infections.

Genetic factors influencing iron storage in humans are identifiable. Iro depletion would be favored by a tendency to heavier menstrual bleeding or b hemophilia. Iron overload is seen in hemochromatosis and in treated thalassemia

We are now in a position to construct a model in which a human populatio group could be distributed along two genetically-determined axes simultaneously one representing gradations in susceptibility to amebiasis determined by non nutritional genetic factors; the other representing iron storage tendencies in th population (Figure 6). The latter, by extension of the previously developed argu ment, should represent a distribution of amebiasis susceptibility/resistance. Give two presumably independent, genetically-influenced schemes, random assortmen would provide for individuals: 1) with a combination of nutritional and non-nutri tional resistance factors; 2) with a combination of nutritional and non-nutritiona susceptibility factors; and 3) many individuals in whom the non-nutritional an nutritional genetic influences would act in opposite directions.

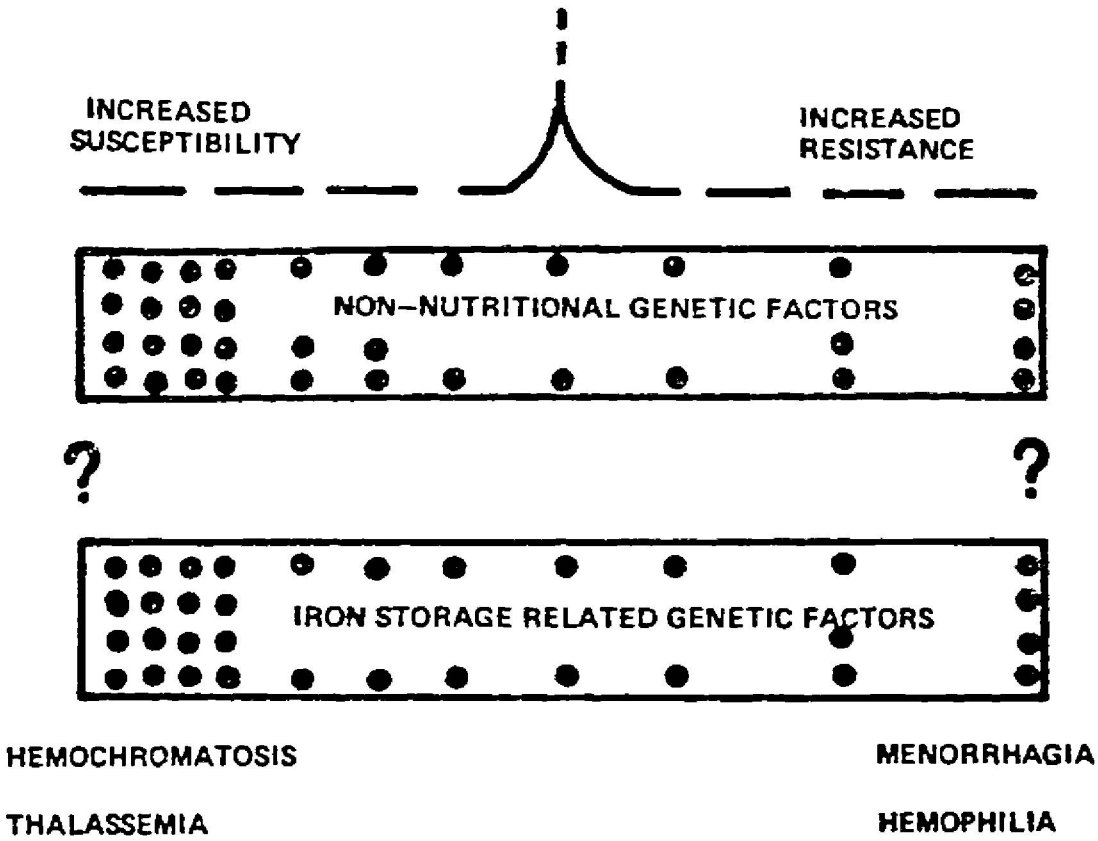

Figure 6. Interplay of non-nutritional genetic factors and specific genetic factors related to iron-storage in the development of increased resistance (right-hand direction) or increased susceptibility (left-hand direction) to severe amebiasis in humans. The non-nutritional factors remain to be defined (? . . . ?) (above), but the tendency toward iron overload and iron depletion (below) are suggested as nutritional determinants.

Limitations to the Study of the Parasitism-Nutrition Interaction

It is important to point out the various barriers, limitations and pitfalls in the investigation of human genetics and human nutrition. Progress in understanding of the interaction of nutrition and parasitism has been hampered not only by its lack of recognition, but also by conceptual and technical limitations.

The diagnosis of human parasitic infections is often elusive. There are, for instance, three species of *Entamoeba* capable of forming four-nucleated cysts: *E. histolytica, E. hartmanni* (small race), and *E. histolytica*-like ameba (low temperature strains) [42]. Only *E. histolytica* is virulent, capable of causing disease in man. Serological diagnosis is notably unreliable for identifying active cases of amebiasis [18]. The only reliable diagnosis rests on the identification of the motile *trophozoite* by an experienced morphologist.

The diagnosis of giardiasis by examination of fecal specimens has a low sensitivity. Alternative, and more reliable, techniques involve a peroral intubation procedure of one form or another: 1) intestinal biopsy; 2) duodenal aspiration

string test. Fecal analyses often miss up to 50% of the cases of giardiasis identified by means of one or the other techniques for sampling the contents of the upper small intestine. Field studies that rely on stool diagnosis alone, suffer from poor sensitivity, while the widepread application of intubation procedures for survey purposes would face problems of compliance.

Even when the infection can be detected, *quantitative* assessment of the parasitic burden of the host is problematic. Too often, reports have provided only *qualitative* results from stool examinations [43, 44]. Whenever possible, the reporting of protozoa or ova in the stool should be expressed per gram of feces. In the case of *Ascaris* quantitative egg counts based on a 24 h fecal output can be related to the number of female worms present in the intestine; the practical problems in obtaining 24-h stool collections in the field, however, are formidable. Alternatively, some investigators have collected information on the number of roundworms passed after chemotherapeutic purging to develop a retrospective estimation of the original worm burden [45, 46]. For parasites such as *S.mansoni,* which do not reside within the interstinal lumen, but rather in the intestinal wall and mesentery, the number of eggs in excreta does not necessarily reflect the burden of mating pairs within the host.

Sound approaches to the nutritional assessment that accompanies studies of parasitic effects are important. This has been especially prominent when growth has been the index criterion. One study of the effect of treatment for ascariasis on nutritional status [47] used an observation period of only 6 weeks; this is hardly sufficient time for marked divergences in growth curves to become manifest. Another such investigation employed an adequate observation interval, one year, but the criterion for improvement or deterioration of nutritional status was a change of only one per cent from the initial height-for-weight classification [48]. If a more generous margin, e.g. two per cent, is applied to the data in the Gupta study [48], all apparent statistically significant differences due to treatment disappear.

Finally, the framework of the concepts of synergism and antagonism in nutrition: infection interactions are based on infections with a single strain of organism [16, 17]. This can be established in a laboratory model, but the reality in free-living human populations is one of polyparasitism. Infected individuals most often have multiple parasites [44, 49], and often both intestinal and blood-borne species are present. Keusch and Migasena [50] have characterized the situation in the following way:

> "Polyparasitism appears to be the rule, rather than the exception, both in populations and in individuals in developing countries of the world. Thus, polyparasitism represents coendemicity in the epidemiological sense and simultaneous infections in individual patients in the clinical sense."

Theoretically, the behavior of a given parasite when present alone may be quite different from its impact when the host has other parasitic infections. Accounting for the influence of accompanying parasites on both the clinical

and epidemiological aspects of the nutrition: parasitism interaction is a severe challenge for future research. To date there are preliminary indications of interactions *between* parasites that might have nutritional consequences. Murray *et al* [51] suggest that *Ascaris* infection tends to *suppress* the expression of *Falciparum* malaria, and speculate that this is mediated through an effect on one or more nutrients essential both to the host and the *Plasmodium*.

Thus, it is important that investigators be able to identify with certainty the presence of parasites, to determine how many parasites, and measure the nutritional status in reliable and precise terms. It is not inconceivable that the biological relationships between nutritional variables and pathogen variables involve *thresholds* of parasite loads, below which no adverse nutritional consequences are to be expected. And finally, the reorientation of research to include more holistic perspectives of the zootic environment of the subjects under study will be important for the interpretation of those former studies which have purported to study single strains of parasites.

CONCLUSION

There are a host of identifiable genetic factors in the expression of nutritional requirements and in the susceptibility to and resistance to parasitic infections. Many more relationships with genetic factors remain to be uncovered. The genetic implications become all the more intriguing in this area because of the complex, bidirectional synergistic and antagonistic interactions between nutritional status and parasitic infection. As illustrated by two simple hypothetical examples presented in this paper, the fact of a triangular interaction matrix among genetic, nutritional and parasite factors makes for rich, conceptual possibilities in scientific investigation. However, profound public health consequences may also be discovered. The investigation of human parasitic infection and its relationship to nutrition is fraught with pitfalls and technical limitations, but careful attention to detail and interpretation of the quasi-experimental designs should allow major new advances in our understanding of the interaction of genetic factors with infectious and nutritional variables in human population that will benefit both scientific knowledge and the quality of life in developing countries.

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DISCUSSION[1]

Lisker asked if iron stores are a factor in susceptibility to amebiasis, is there a discrepancy between the incidence in males and females, especially after puberty? Solomons replied that the data necessary to answer that question were not available. Scrimshaw thought Solomons may have oversimplified the relationship between iron intake and parasitic infestation. The effects of iron supplementation have been seen primarily in hosts immunocompromised as a result of malnutrition. In this case, iron may facilitate replication of a parasite or microbe prior to the hosts regaining immunocompetence. Parasitic disease is hard to look at separately from bacterial or viral disease, since both are prevalent in the same individuals.

[1]*Summary of the discussion prepared by S. Cederbaum.*