values for nonpregnant anemic subjects and are one-quarter the calculated absorption in the four nonpregnant subjects reported in this study. Neither folate nor B_{12} was limiting in groups one through five. Were there physical or dietary conditions which limited iron availability, absorption or hemoglobin synthesis in these village women? While the answers are not known, reports of disappointing hematologic responses to supplemental iron in gestational anemia in other countries are cited by the authors.

From a public health point of view, the persistence of a high frequency of anemia in spite of supplementation programs raises the traditional Procrustean dilemma in allocation of limited resources: whether to identify and treat the most severely anemic pregnant women (a logistically complex and expensive intervention mode) or whether to supplement the whole population at risk even though oral hematinic therapy is demonstrably incapable of reversing or even significantly mitigating the condition?

This also touches upon a further problem: does "borderline" anemia, in contrast to "severe" anemia, really impair health in any demonstrable way? If so, it has so far eluded detection and quantification. In an earlier review[2] the failure to relate various middle-aged health-related symptoms to hematologic values was reviewed. More recently, Elwood[3] was unable to associate hematocrit, in the borderline area, with mortality in 18,740 women. The classic Vanderbilt study[4] failed to show a relationship between maternal hemoglobin level and outcome variables such as birth weight, infant hemoglobin or risk of anemia in the first year of life. This comparison involved the lowest and highest hemoglobin quartiles, group mean hemoglobins being 9.9 and 13.1 g per 100 ml respectively.

Thus the functional impact of gestational anemia is not clear, nor has the health impairment associated with suboptimal iron nutriture among adults been clearly demonstrated. □

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IMMUNE DEFICIENCY IN MALNUTRITION

Once again it is shown that a defect in cellular immunity exists in malnutrition. The clinical significance of such a finding is that malnourished children may be more prone to fungal and gram-negative infections.

Key Words: immune competence, malnourished, immunoglobins, cellular immunity, immunodeficiency

There are now several studies which document the relationship between malnutrition and infection.[1,2] Scrimshaw and his colleagues, who perhaps have done the most to promote this association, commented in detail on the vicious cycle which may be set in train when malnutrition predisposes to infection which in turn produces a greater degree of malnutrition.[3,4] The major reason for newer studies would be to use newer tests of immune competence or to identify various aspects of the malnutrition process which may be more specifically related to immunodeficiency. The study of Smythe et al., which has already been reviewed,[5] presented data partly based on autopsy material showing that

there was a defect in cellular immunity. More recent work showed that there may be a specific T cell abnormality.[6]

A recent study on Ghanaian children presents further detailed evidence of a defect in cell-mediated immunity.[7] In addition an attempt was made to find meaningful correlations between various indices of malnutrition and measures of immune competence. One hundred and seventeen children were divided into three groups. There was a group of controls which consisted of children above 81 percent of the Harvard standard, had normal serum protein levels and were normal at clinical examination. The malnourished children were divided into two groups on the basis of clinical examination, anthropometric and laboratory data. The group of severely malnourished children could be divided into those with marasmus and those with kwashiorkor, but all were less than 60 percent of the Harvard standard. The group with moderate malnutrition was 61 to 80 percent of the Harvard standard and came from nutritional rehabilitation units.

Clinically obvious infections were most common in the severely malnourished children; 18 percent had skin fungus and 15 percent had pneumonia. Pyoderma occurred in all groups of children. It was striking to note that 3 percent of the severely malnourished children had tuberculosis. Infestation with Strongyloides stercoralis was ten times more common in the severely malnourished compared with other children, but ascariasis and giardiasis were equally frequent in all groups. Clinical assessment of tonsil size showed that in 36 percent of the malnourished children the tonsils were not visible or barely visible and in general, the better nourished the children, the larger the tonsils. As perhaps could be predicted, plasma proteins were lowest in the severely malnourished children. The depression of serum albumin and transferrin was most marked in children with kwashiorkor.

Levels of the third component of complement were significantly reduced in the severely malnourished group and this was also most marked in children with kwashiorkor. It took only two weeks of nutritional rehabilitation for C_3 to increase to normal levels. The levels of all five immunoglobulins were elevated in all the Ghanaian children when the values were compared with those from American children. A comparison within the three groups of Ghanaian children showed that the immunoglobulins were highest in the most severely malnourished children. An interesting observation was that Ig^E was most markedly elevated in children with intestinal parasites. Malnutrition did not affect the antibody response to keyhole limpet hemocyanin and polyvalent pneumococcal polysaccharide.

The most impressive finding in this study was the depression of the cellular immune response. The mean absolute lymphocyte count and cutaneous delayed hypersensitivity to phytophaemagglutinin, monilia streptokinase-streptodornase were significantly reduced in severely malnourished children. The in vitro lymphocyte reactivity to phytohaemagglutinin was significantly reduced in both groups of malnourished children with the severely malnourished ones showing the greatest reduction.

The authors give detailed statistical correlations between several of the things they measured. Tonsil size and the indices of cellular immunity showed correlations with total serum proteins, albumin, carotene, hemoglobin and vitamin C levels. The anthropometric measurements such as weight for age, arm circumference and triceps skin fold showed impressive highly significant correlations with the indices of cellular immunity but also with the serum transferrin; arm circumference and skinfold thickness were correlated with the serum complement.

This study confirms previous ones which showed depression of cellular immunity in malnutrition.[1,2,6] In addition, it shows that the extent of the depression is related to the severity of the malnutrition. The authors do point out that malnutrition is

associated with multiple deficiency states and it is impossible to single out one as being primarily responsible for any immunodeficiency. Iron deficiency for example which is a common finding in malnutrition is often associated with cellular immunodeficiency.[8] The question must now be asked, what is the effect in clinical terms of this immunodeficiency? It is constantly stated and the authors repeat it, that these immunodeficiencies make the malnourished child more prone to infections with gram-negative organisms. The authors also imply that this finding of a low C_3 may be of significance in this regard.

It should be pointed out that it requires much more evidence beside a depression of C_3 in the presence of a normal C_4 to allow any opinion to be given on the functional state of the complement system as a whole or of any of the component parts. Unfortunately the evidence for a greater prevalence of gram-negative infections in malnutrition is represented by a few limited studies.[9,10] From the authors' own data pneumonia was the most common infection and there is no evidence that pneumonia with gram-negative organisms is more frequent in malnutrition.

The evidence that malnutrition and infection go hand in hand is indeed strong, but perhaps the time has come for attention to be paid to the ecological aspects of the two. The association is not surprising when children who are malnourished often live in the kinds of unsanitary and overcrowded conditions which are the natural breeding grounds of infection. Tuberculosis is common in malnutrition, but the evidence is strong that this infection thrives among people in poor living conditions. Pneumonia is common in malnourished children, but is it the result of a basic immune deficiency or does poor hygiene plus the general weakness and inability to cough properly help in making the child prone to all respiratory infections? The authors point out that skin fungus infection was most common in the severely malnourished child, but this could also be attributed to a lack of basic sanitation rather than to an immunodeficiency. The mucocutaneous candidiasis which can be seen in cellular immune deficiency states has not been recorded in protein-energy malnutrition.

It is surprising that in a study such as the present one no mention was made of the work in Uganda[11] which showed the relationship of infection to malnutrition most elegantly. Episodes of infections occurred while children were relatively well nourished, but because of the convalescent anorexia coupled with the relative unavailability of excess food these children could not exhibit the normal catch-up growth which follows any period of growth failure. These children because of repeated infections showed progressive falls in serum albumin and slow development of clinically obvious kwashiorkor.

From the practical clinical aspect of the treatment of malnourished children, the most important point is not simply the frequency of infections with which the child presents, but the fact that it is very difficult to diagnose these infections. Leukocytosis and pyrexia may be absent, Mantoux tests may be invalid and a high index of suspicion must always be maintained. □

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