The interaction of nutrition and infection: A succinct review

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Malnutrition combined with susceptibility to infection threatens the health and survival of a large portion of the world’s population. Of the many components of the host-parasite relation, nutrition has not received the attention it deserves. There has been increasing activity in recent years on the elucidation of the role nutritional factors play in the behavior of both host and parasite.

This paper reviews the effects vitamins exert on the course of parasitic infections.

Nutrition and Parasitic Infections

Host-parasite relationships have long presented interesting problems to biologists. The theoretical ideal is that under natural conditions, host animals and their parasites have evolved in such a way that no harm is caused to the host by the parasite. This ideal equilibrium is soon upset in both man and domestic animals living under unnatural conditions, and disease then becomes a serious problem. According to Hunter, parasites of man are fewer in countries where modern sanitation prevails. In other countries overcrowding, lack of sanitation, poor nutrition, and many other circumstances have upset the supposed equilibrium; parasites multiply out of proportion to the human population and cause much disease and economic loss.

Nutrition exerts profound influences on the course of parasitic infection. The resultant effects may be divided into two general categories: those in the parasitic bed, or what may be termed in vivo culture conditions, and those in the defense mechanisms of the host.

Nutritional Influences on the Parasitic Bed

In vivo parasites are influenced by: (1) lack of substances required by the parasites; (2) presence of substances having specific stimulating effects on parasites; (3) presence of substances detrimental to parasites; and (4) indirect affect on the parasite environment and changes in the metabolism of the host affecting hormones and enzymes.

Helminths

Among the first studies on vitamin deficiency and helminthic infection were those by Zimmerman et al. These workers observed that young chicks deficient in vitamin B were less resistant to parasitism by Ascaridia perspicillum; the deficient chicks having more and larger worms than non-deficient chicks. A similar observation was made in chicks deficient in vitamin A and infected with Ascaridia lineata and in vitamin B-deficient chickens that were given the same number of embryonated eggs of A lineata as the adequate-vitamin B controls. Ackert and Spindler noted that vitamin D-deficient chicks infected with A lineata gained less weight than the controls. Wright found that the average number of ascarids per dog on a vitamin A-deficient diet was about five times that of dogs on a normal diet. Sadun et al reported more and larger worms in folic acid-deficient chicks infected with A galli. McCoy observed that vitamin A-deficient rats showed lowered resistance to Trichinella spiralis infection. Adult worms persisted in the intestine and more larvae encysted in muscles of deficient rats than in adequately nourished controls; the deficient rats developed no immunity to a second infection while the control rats were completely immune. Layrisse et al reported an impairment of folic acid absorption in patients with severe hookworm disease. Spindler reported...
showed that a lack of vitamin A in the diet prolonged the patent period of Nippostrongylus muris in superinfection to 64-67 days whereas the patent period in superinfections of control animals was 11-14 days. In experiments with Strongyloides ratti, Lawler\textsuperscript{14} observed that rats deficient in vitamin A had a lower resistance to primary infection and less immunity to reinfection than nondeficient rats. He suggested that vitamin A was intimately linked with the reticuloendothelial system of the host.

### Protozoans

Protozoal infections have also been shown to be modified by alterations in the vitamin contents of the host. Sadow et al\textsuperscript{22} working with a human strain of Entamoeba histolytica encountered higher infectivity and mortality rates in guinea pigs that were fed a vitamin C-deficient diet when compared with controls. The degree of infection in guinea pigs that were mildly scorbutogenic was intermediate between the nondeficient and deficient groups.

Erasmus et al\textsuperscript{16} reported that chicks on a vitamin A-free diet were more susceptible to infection with Eimeria tenella and Eimeria acervulina than well-fed control animals. Survival rates were enhanced as the level of vitamin A increased.

Brackett et al\textsuperscript{17} found blood-induced infections of Plasmodium gallinaceum were suppressed in pantothenic acid-deficient chicks and in chicks given an oral dose of a pantothenate analogue. Sporozoite-induced infections were not similarly affected by the deficient state. P gallinaceum oocysts in Aedes aegypti and Anopheles quadrimaculatus were increased substantially when folic acid was added to the sugar diet of the mosquitoes.\textsuperscript{18} Ducks deficient in biotin developed more severe infections with Plasmodium lophurae and P catemerium respectively.\textsuperscript{19} Pantothenate deficiency failed to produce the same effect. Seeler et al\textsuperscript{20} recovered twice as many P lophurae organisms in biotin-deficient chicks compared to chicks on an adequate vitamin diet. Contrary to biotin deficiency, riboflavin deficiency decreased the severity of P lophurae infection in chicks. Seeler and Ott\textsuperscript{21} reported similar observations in folic acid-deficient chicks inoculated with P lophurae. Nicotinic acid-deficient chicks show four to five times greater parasitemia than nondeficient birds infected with P lophurae.\textsuperscript{22} Trager\textsuperscript{23} demonstrated that the extracellular development of P lophurae, in vitro, and the intracellular development of P falciparum were enhanced in media containing high concentrations of folic acid.

Actor\textsuperscript{24} studied the effects of pyridoxine, pantothenate, and thiamine in mice infected with Leishmania donovani and showed that late in the infection, more parasites accumulated in the livers and spleens of pyridoxine and pantothenate-deficient mice than control animals. Thiamine deficiency did not produce any significant differences in the infection.

Caldwell and Gyorgy\textsuperscript{25,26} reported lowered resistance to Trypanosoma lewisi infection in rats deficient in biotin. Yaeger and Miller\textsuperscript{37-39} demonstrated that, except for riboflavin deficient animals, rats deficient in thiamine, pantothenate, pyridoxine, biotin, and vitamin A were more susceptible to T cruzi infection than control animals. Lee\textsuperscript{30} observed higher parasite counts and a longer survival rate in the mice deficient in pantothenic acid and infected with T duttoni.

In a series of studies, Aboko-Cole and Lee\textsuperscript{34,35} investigated the effects of folic acid on T lewisi and T rhodesiense infection in rats fed complete, folic acid-deficient and pair-fed control diets. Irrespective of diet, the infected animals consumed more food and gained more weight than the uninfected animals. Rats deficient in folic acid had twice as many trypanosomes as the nondeficient control rats. Infected rats, regardless of diet, showed higher liver mitotic activity than uninfected rats. The infected rats, regardless of diet, had serum folate levels of over 100 percent when compared with controls. The increase in vitamin level was, however, greater in the deficient, infected rats, ranging up to 400 percent over uninfected controls. Livers of deficient, infected rats showed significantly higher folate levels than those of uninfected rats. Brains and spinal cords of T lewisi-infected, folate-deficient rats showed no significant difference in folate content. However, those of T rhodesiense-infected, folate-deficient rats contained significantly more folic acid than the uninfected rats. T lewisi infection does not cross the blood-brain barrier while T rhodesiense crosses the barrier to reach the spinal cord and brain.

### Nutrition and Bacterial and Viral Infections

The normal course of bacterial and viral infections may also be altered when vitamins are eliminated from the diet of the host. Rats on a vitamin A-free diet were markedly more susceptible to infection by Salmonella enteritidis than well-fed control rats.\textsuperscript{28} Kliger et al\textsuperscript{39} found that starvation, rather than vitamin-A deficiency, was responsible for the lowered resistance in rats and mice infected with Salmonella typhimurium. Kliger et al\textsuperscript{39} showed that biotin-deficient rats and mice were more susceptible to S typhimurium infection than control animals. Guggenheim and Buechler\textsuperscript{31} found that susceptibility was secondary to anorexia in rats deficient in thiamine and infected with S typhimurium. In mice, however, low resistance was the result of thiamine deficiency.

In contrast to rats on a vitamin D-deficient diet, Boynton and Bradford\textsuperscript{40} showed that rats deficient in vitamin A readily succumbed to infections with a bacillus of the Muscosus capsulatus group. Robertson and Ross\textsuperscript{41} increased the resistance of rats to a "rat typhoid infection" by adding vitamin A to their rachitogenic diet. Zucker and Zucker\textsuperscript{42} demonstrated that rats deficient in pantothenic acid may lose the inherent species-determined resistance to infection with a corynebacterium known only to be pathogenic for mice. Similarly, Haltalin et al\textsuperscript{43} reported that folic acid deficiency caused the naturally resistant guinea pig to become fatally susceptible to Shigella flexens infection.

Guggenheim and Halevy\textsuperscript{44} reported that rats deficient in thiamine and infected with Borrelia persica, the spirochete of relapsing fever, showed a larger duration of infection and higher fatality rate than the controls. The reduced resistance was found to be due not only to the vitamin deficiency but also to the resultant decrease in food intake.

Forrer et al\textsuperscript{47} reported that resistance to the murine poliomyelitis virus may be increased if the host's thiamine intake is lowered. Toomey et al,\textsuperscript{48,49} working with the poliomyelitis virus, observed that paralysis developed more quickly in mice that were fed a
vitamin B<sub>1</sub>-complete diet than in those fed a diet deficient in vitamin B<sub>1</sub>. A similar observation was made by Forster et al.<sup>50</sup> who found that mortality rate and incidence of paralysis were lower in mice that were deficient in vitamin B<sub>1</sub> and infected with the Lansing strain of poliomyelitis virus than in the nondeficient animals. Forster et al.<sup>51</sup> studied the effects of vitamin B<sub>1</sub> deficiency and restricted food intake on poliomyelitis in mice and found a slightly greater number of deaths in restricted animals than in vitamin B<sub>1</sub> deficient mice. Lichstein and his co-workers<sup>52</sup> demonstrated that mice fed a pantothenate-deficient diet showed an increased resistance to Theiler's encephalomyelitis virus. Lichstein et al.<sup>53</sup> reported that Rhesus monkeys with chronic folic-acid deficiency were more resistant to poliomyelitis virus than those with acute folic-acid deficiency. Neither mice treated with amethopterin, a folic-acid antagonist, nor mice deficient in folic acid were killed by a normally lethal load of the virus of lymphocytic choriomeningitis.<sup>54</sup> In another study,<sup>55</sup> mice suffering acute deficiency were killed by the virus; however, animals suffering from chronic deficiency survived the infection. The same number of viruses were recovered from brains of treated and untreated mice.

The studies of Axelrod and Hopper<sup>56</sup> showed that antibody production was considerably impaired in pyridoxine-deficient and pantothenic acid-deficient rats infected with the influenza virus; pronounced thiamine deficiency did not seem to affect antibody production. Young mice inoculated with the pneumonia virus of mice and then fed a diet deficient in pyridoxine were more resistant to the infection than the well-nourished controls. Susceptibility to the virus infection increased with increasing pyridoxine administration.<sup>57</sup>

Squibb<sup>58</sup> discovered that 30 times the normal requirement of thiamine, pantothenic acid, niacin, pyridoxine, and biotin, and seven times the normal requirement of B-complex vitamins increased the mortality of chicks infected with Newcastle disease virus from three percent to 13 percent over that of birds with normal body reserves of vitamin. Little et al.<sup>59</sup> concluded that depleted reserves of folic acid may reduce the incidence of Rous sarcoma in chickens.

### Summary

The Darwin-Wallace observations and theories of natural selection did not refer only to environmental changes such as climate or changing landforms; the fight for existence also includes survival from invasion of parasitic birds and other animals as well as survival from attacks of organisms and agents that cause and transmit disease.<sup>60</sup> In the case of disease, self-existence depends on modifying or completely altering the external factors that provide a conducive atmosphere for the propagation of disease and an adjustment of an individual's internal body systems so that it becomes invulnerable to the consequences of invasion. Vitamins are essential among the nutrients that help an individual to maintain functional defense mechanisms.

Each of the studies mentioned above has shown one of the following: 1. that certain nutritional deficiencies increase host susceptibility to infection, ie, antagonism; 2. that certain vitamin deficiencies may enhance host survival, though not necessarily decreasing parasitism, ie, antagonistic cooperation between host and parasite; 3. that, in some infections, increases in certain vitamin concentrations may increase the mortality rate of the host, ie, another form of antagonism.

An understanding of the actual processes that regulate the metabolism of the parasite and the infected, deficient host may lie in (1) the identification of components that may be common to groups of vitamins that produce adverse and/or beneficial effects during infection; and (2) the identification of other nutrients that may be suppressed or inactivated and may provoke an imbalance in metabolism by reshuffling and substituting functions.

### Literature Cited

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