Chapter 9

The Ecology of Poverty: Nutrition, Parasites, and Vulnerability to HIV/AIDS

Eileen Stillwaggon

HIV/AIDS continues to spread throughout the developing world, in transition countries, and among poor and marginalized populations in industrialized countries. In its third decade, and even with increased resources, global AIDS policy is still failing to stem the epidemic. HIV prevention fails because it ignores the fundamental causes of the epidemic, it is unscientific, and it attempts to intervene at the last minute with programs limited to behavior change.

The HIV epidemic is not an isolated event. It is the predictable result of declining economies, insecure food systems, and inadequate investment in water, sanitation, health care, and education. The crisis of sustainable agricultural systems, most notably in Sub-Saharan Africa but elsewhere as well, has aggravated the health crisis in developing countries and favored the spread of HIV. The collapse of agricultural economies caused rapid urbanization, unemployment, and increasing inequality. The AIDS literature addresses, to some extent, the effect of economic crisis on behavior through the disruption of relationships and through pressures toward unsafe sex, in particular in the form of commercial sex for survival. Little emphasis, however, has been placed on the direct, biological effects of malnutrition and unsanitary conditions on the vulnerability of individuals and societies to HIV.

The epidemic of HIV cannot be explained by behavioral factors alone, even though a necessary condition is contact through sex, needles or other medical instruments, or mother to child. Scientific evidence demonstrates the role of biological cofactors such as malnutrition and parasitic and infectious diseases in enabling the transmission of HIV. Although AIDS policy organizations use the phrase, "AIDS

is a development issue," they do not incorporate scientific information about the diseases and conditions of poverty into their programming for HIV prevention. Consequently, their policies are limited to programs that address only behavioral factors. This chapter integrates analysis of poverty with the epidemiology of infectious and parasitic diseases. Combining medical, economic, and geographical data, it demonstrates the specific disease synergies that promote HIV transmission in poor populations.

How Diseases Spread

An individual's vulnerability to any disease depends on the strength of the immune system, which is affected by nutrition, stress, and the presence of other infections and parasites, as well as other factors. Transmission of a disease also depends on the virulence of the pathogen. HIV has a very low probability of transmission between otherwise healthy adults: one in 1,000 contacts from women to men and one in 500 contacts from men to women (World Bank 1997). The low probability of transmission between healthy adults, however, has little applicability among poor people in Sub-Saharan Africa, Asia, Latin America, and transition countries because they are already immunocompromised as a result of malnutrition, parasites, or other infections. The risk of infection with HIV is greater than that in well-nourished, healthy populations, not only because of higher prevalence of HIV in the population but also because of the prevalence of those cofactor conditions that decrease immune response in HIV-negative persons and increase viral load in HIV-infected persons. Infectious and parasitic diseases and malnutrition create an environment of risk. In a risky environment, the likelihood of infection with HIV is greater with each sexual contact, regardless of the number of contacts.

Malnutrition

Probably the most fundamental cause of the widespread epidemic of HIV, particularly in Sub-Saharan Africa, is the failure of agricultural systems and food supply. Food insecurity has promoted the spread of HIV both indirectly, through migration and the resort to risky behaviors, and directly, through its biological effect. Malnutrition undermines the immune response, directly increasing vulnerability to disease.

Epidemiology has long recognized the importance of adequate nutrition for protection from disease. In the late 1960s, the World Health Organization officially acknowledged the important synergies between malnutrition and infection. With the advances of molecular biology of the past several decades, it is possible to see

the specific mechanisms by which overall malnutrition and micronutrient deficiencies weaken the immune system. That weakened immune response makes people more vulnerable to all infectious and parasitic diseases, regardless of whether they are transmitted by water, food, air, soil, or sex.

Increased susceptibility to infection results from both protein and energy malnutrition (macronutrition) and deficiencies of specific micronutrients, such as iron, zinc, and vitamins. Infection and malnutrition are synergistic; minor illnesses can cause lack of appetite, which is very dangerous in a person who is already nutritionally deficient and parasite-laden. Fever increases the demands for energy at the same time that intake decreases. Diarrheal diseases cause a rapid loss of nutrients (Scrimshaw and SanGiovanni 1997).

Both undernutrition and micronutrient deficiency, even in the absence of readily observable symptoms, weaken every component of the immune system, both its adaptive and nonadaptive responses. Numerous studies have demonstrated the effects of even moderate protein-energy malnutrition (PEM) on the physical barriers, epithelial (skin) and mucosal protection (Woodward 1998). The humoral response is also affected through atrophy of the lymph system, and reduction in size and weight of the thymus results, affecting T-cell production (Beisel 1996; Chandra 1997). Children with PEM, regardless of degree or type (stunting or wasting), have reduced cell-mediated adaptive immunity (Chandra 1997; Woodward 1998). Protein is very important in resistance to infection because most elements of the immune system depend on cell replication, which requires protein (Scrimshaw and SanGiovanni 1997). Protein deficiency has been shown to impair resistance to tuberculosis, for example, by preventing containment of the mycobacteria within the primary lesions (McMurray 1998).

Micronutrient deficiencies also weaken every component of the immune system, even when deficiencies are relatively mild (Chandra 1997). Some diseases, such as scurvy (from vitamin C deficiency) and pellagra (from a lack of niacin, a B vitamin), result from specific nutrient deficiencies. Besides their role in deficiency-specific diseases, many nutrients are needed both singly and in conjunction with others to maintain an immune system that can resist the entire array of infectious, parasitic, and even chronic degenerative diseases. Iron-deficiency anemia, for example, is the most widespread nutritional deficiency in the world and is especially common in women and children. Iron is essential in promoting resistance to infection through humoral response (B cells), T cells, and NK cells (Scrimshaw and SanGiovanni 1997).

Even mild zinc deficiency can cause a large decrease in natural killer cell activity and reduced production of thymic hormone, affecting T-cell production (Beisel 1996; Cunningham-Rundles 1998). Zinc deficiency also impedes wound healing,

undermines skin integrity as a barrier to infection, and weakens resistance to parasite infection, which aggravates malnutrition (Chandra 1997). Zinc deficiency is a common result of prolonged diarrhea; supplementation reduces diarrhea and is a low-cost way to reduce malnutrition and boost immune response (Ruel et al. 1997).

Vitamin A deficiency reduces the number of natural killer cells, diminishing nonspecific, or natural, defense mechanisms against antigens. Vitamin A also is required for the production of T cells, or specific defenses. Insufficiency of vitamin A is the deficiency that is most synergistic with infectious disease (Semba 1998). Infection increases excretion of vitamin A, producing a deadly synergism of malnutrition, infection, and increased vitamin A deficiency (Stephensen et al. 1994). Even children with subclinical vitamin A deficiency show a reduced immune response and greater vulnerability to infection, particularly of the skin and mucous membranes (Solomons 1998). Subclinical vitamin A deficiency is more likely to occur in children who also show signs of PEM (Khandait et al. 1998).

Vitamin A is particularly important in the promotion of physical barriers to infection. Vitamin A deficiency disturbs the integrity of the skin and mucous membranes and permits the invasion of pathogens in the eyes, the respiratory system, and the genitourinary and digestive systems (Semba 1998). Vitamin A deficiency also impairs iron utilization and so interacts with anemia (Sommer et al. 1996). Supplementation with vitamin A along with iron can eliminate anemia. Supplementation with vitamin A is very low cost, and its cost-effectiveness is enhanced because of its interaction with iron.

Nutritional deficiencies interact with parasite infection to make a combined assault on nutrition and immune support (Friedman et al. 2003). Vitamin A supplementation is an effective low-cost strategy to reduce malarial illness in young children (Shankar et al. 1999). Interventions that address nutritional deficiencies and parasitic infection are important for their own sake and for HIV prevention, especially because blood transfusions are a common therapy for malaria, which is endemic in areas where blood supplies may also be unsafe (Hedberg et al. 1993).

In sum, overall malnutrition combined with micronutrient deficiency is widespread in Sub-Saharan Africa, South Asia, and elsewhere among very poor people and is responsible for suppression of immunity through all three routes: physical barriers, humoral immunity, and cell-mediated immunity. In particular, vitamin A deficiency produces a greater susceptibility to STDs, particularly of the ulcerative type, in malnourished populations in tropical areas. It is important to reiterate that STDs (including HIV) are not a special case; they are infectious bacterial and viral diseases that can most easily be transmitted to a host whose immune system is

weakened by malnutrition and by the synergistic effects of other infectious and parasitic diseases. STDs find their most fertile ground in the most nutritionally immunosuppressed population, such as we find in many countries in Africa and Asia. In particular, malnutrition that disturbs epithelial integrity promotes access for any disease, including genital ulcer diseases that provide entry points for HIV.

Maternal malnutrition in general and deficiencies of specific micronutrients, such as vitamin A, are associated with greater risk of vertical (mother to child) transmission of HIV. In Malawi, it was observed that mothers severely deficient in vitamin A had a much higher risk of transmitting HIV to their children, perhaps because of its effect on the vaginal mucosa or the integrity of the placenta (Semba et al. 1994; Nimmagadda, O'Brien, and Goetz 1998). Increased viral load in the mother and decreased maternal antibody protection, both associated with impaired T- and B-cell production from vitamin A deficiency, are also probable causes of greater transmission (Landers 1996). Randomized trials in Tanzania found that multivitamin supplementation decreased fetal deaths and increased T-cell counts in HIV-infected mothers (Fawzi et al. 1998). Nutritional supplementation of mothers was expected to reduce vertical transmission by reducing viral load in secretions in the birth canal and in breast milk (Fawzi and Hunter 1998). Although recent trials of vitamin A supplementation have not yet been successful in reducing vertical transmission, they suggest useful avenues for research. The environment of poverty, malnutrition, and parasitosis in which HIV flourishes provides a complicated laboratory for trials of any single intervention. Complementary interventions in malaria treatment or other nutritional supplements might be necessary in order to detect the effectiveness of vitamin A supplementation for HIV prevention in this multiburdened population.

Systemic maternal virus burden is an important factor in HIV transmission to infants. Local virus burden (in the birth canal), however, may be even greater than systemic viral load, and therefore, measures of systemic viral load might understate the risk of vertical transmission. Anemia is associated with greater viral shedding, with consequent locally higher viral burden in the birth canal, increasing the risk of transmission from mother to child, which could be remedied with nutritional supplementation (John et al. 1997).

Malnutrition in its various forms promotes viral replication and consequently can contribute to greater risk of vertical or sexual transmission (Friis and Michaelsen 1998). Supplementation improves health outcomes for HIV-infected persons, including children. In addition to helping people living with HIV, the reduction in viral load from improved nutrition reduces the risk of transmission for children and adults.

Parasitic Diseases

The economic crisis in developing countries and the austerity policies that were subsequently enforced contributed to the neglect of sanitary infrastructure and programs to eradicate parasitic and infectious diseases. Development policies in most countries ignored the crucial role of good health not only for human development but also for the economic viability of poor countries. Populations burdened by parasites cannot learn or work to their full capacity and are more susceptible to epidemics, such as that of HIV/AIDS.

Parasitic and infectious diseases interact with malnutrition. Malnourished people are more vulnerable to those diseases, and their illnesses are more severe than those of well-nourished people. Parasites also aggravate malnutrition by increasing calorie requirements and draining nutrients. Through their effect on malnutrition and through specific synergies with HIV transmission detailed below, parasitic diseases increase the spread of HIV/AIDS.

Malaria

Malaria is caused by a protozoal parasite spread by mosquitoes. The endemic zone of malaria is increasing as a result of lack of control efforts and perhaps also climate disturbance from global warming. Over 300 million people in Africa suffer from acute malaria each year, and almost one million children in Africa die of malaria annually. Malaria is also implicated in the spread of HIV in Sub-Saharan Africa.

Malaria stimulates HIV replication, and HIV viral loads (the amount of virus in the blood, semen, or other body fluid) are significantly higher in malarial patients than in HIV-infected persons without malaria. The higher HIV viral load in malarial patients, even after four weeks of treatment for malaria, suggests that malaria could cause faster progression of HIV (Whitworth et al. 2000). High viral load as a result of malaria coinfection correlates with risk of HIV transmission through blood, from mother to child, and through sexual contact. In Malawi, men with malaria were found to have seven times the median viral load of HIV-infected men without malaria. The reduction in viral load that results after treatment for malaria indicates that the causation is not from higher viral load to malaria but rather from malaria to higher viral load (Hoffman et al. 1999).

HIV-infected persons also have higher malaria-parasite densities in their blood, which increases the likelihood of malaria transmission in a population with high HIV prevalence (Whitworth et al. 2000; Rowland-Jones and Lohman 2002). The greater prevalence of malaria and the higher parasite loads both mean that HIV also promotes malaria transmission. Malaria is a very serious health problem in the developing world, especially in Sub-Saharan Africa. Malaria control is essential for reducing HIV transmission in children and adults through its effect on viral load

for mothers and for sexual partners (Corbett et al. 2002). Controlling malaria would also alleviate one of the world's most devastating health problems.

Helminthic and Filarial Infections

Poor communities lack sanitary facilities for disposal of human waste, which perpetuates the cycle of contamination of soil with numerous kinds of worms. Lack of easy access to clean water makes it difficult to keep hands and food preparation areas clean. Consequently, soil-transmitted helminths are virtually ubiquitous in shantytowns, rural communities, and even among more affluent urban residents in many countries. Nearly 1.5 billion people are infected with ascariasis, 1.3 billion with hookworm, and over 1 billion with trichuriasis (PPC 2002). Worms cause malnutrition, even in adequately fed persons, because they drain the food supply through diarrhea, and they cause anemia from intestinal bleeding. They also weaken immune response because the immune system is exhausted from chronic reaction to the nonself invaders. Helminthic and filarial infections have also been shown to increase susceptibility to HIV acquisition and likelihood of transmitting HIV.

One of the reasons that ubiquitous health conditions, such as worm infection, are overlooked as cofactors is frequently the lack of a control group. In developing countries, virtually everyone harbors at least one parasite, so it is almost impossible to conduct research on a population not affected by endemic parasitic disease. By comparing recent immigrants from Ethiopia with earlier immigrants from Ethiopia and elsewhere, a team of Israeli researchers has shown that immune activation of the host caused by endemic infections, particularly helminthic (worm) infections, makes the host more susceptible to HIV infection and more vulnerable to HIV replication once infected (Bentwich et al. 1999). More than 80 percent of immigrants they studied had at least one helminthic parasite, 40 percent had two parasites, and 3 percent were infected with four different intestinal parasites. Even those who were HIV-negative and TB-negative evidenced broad immune dysregulation (Borkow et al. 2000). Blood cells taken from HIV-negative but helminth-infected subjects were highly susceptible to HIV. In addition, treatment for helminths reduced HIV plasma viral load in HIV-infected persons (Bentwich et al. 1999). HIV viral load is greater in people from developing countries and is positively correlated with helminth load. Helminths impair immune response, but treating people for worms enables immune response to recover (Borkow et al. 2001). Deworming is cheap, effective, and easily tolerated.

Filaria worm infection is also endemic in countries throughout Asia, Africa, and the Americas, and filariasis is also implicated in greater transmission of HIV. Blood cells of people infected with filaria worms and exposed to HIV show higher levels of HIV proliferation compared to blood cells of healthy persons similarly

exposed in vitro. Furthermore, blood cells taken after patients are treated for filarial infection are less susceptible to HIV infection. People infected with worms very likely have increased susceptibility to HIV infection, and "aggressive treatment and control programs for filarial diseases and possibly other helminth infections in areas of Africa, India, and Southeast Asia where the HIV epidemic is rampant" are necessary (Gopinath et al. 2000).

Genital Schistosomiasis

Schistosomiasis is a parasitic disease second only to malaria in its prevalence. It affects more than 200 million people in 74 countries (WHO 1996/2003). Of the five species of waterborne schistosome flatworms, *S. hematobium* is more common in Sub-Saharan Africa than in other regions. Dam construction has caused an increase in schistosomiasis prevalence in a number of African regions, including a threefold increase in some countries (Sharp 2003).

People become infected with schistosomiasis when they are in contact with fresh water in lakes and slow-moving streams infested with snails that harbor the schistosome worms. The worms enter through the skin and locate in the intestines (*S. mansoni* generally) or the urinary tract (*S. hematobium*). The worms leave eggs that further infect those regions. Because people use such streams for bathing, washing clothes, recreation, or collecting aquatic plants for food or thatching houses, schistosome infection is widespread.

With the possible exception of malaria, schistosomiasis, also known as bilharzia, is probably the most significant parasitic cofactor of HIV transmission because some schistosome species colonize the genitourinary tracts. Urinary and intestinal schistosomiasis are generally the more recognized variants, but the importance of genital infection with schistosome worms and eggs has been known for decades. The interaction of female genital schistosomiasis with and contribution to HIV transmission was clearly described as early as 1995 (Feldmeier et al. 1995) and has been demonstrated in numerous studies reported in scientific journals since then, and yet schistosomiasis treatment and eradication are not addressed in HIV-prevention programs. The coincidence of schistosome-endemic areas with zones of high HIV prevalence provides epidemiologic support for a biological mechanism by which the parasite increases vulnerability to HIV transmission (Harms and Feldmeier 2002). Schistosomiasis is so highly endemic that it can be overlooked as a cofactor for other locally endemic conditions.

Prevalence in endemic zones is extremely high. In one endemic area of Tanzania, for example, 63 percent of residents were infected with *S. hematobium,* and 34 percent with *S. mansoni* (Poggensee et al. 2000). Sixty to 75 percent of women with *S. hematobium* (urinary) have genital manifestations, with infestation of worms

and ova in the vagina, uterus, vulva, or cervix (Feldmeier, Helling-Giese, and Poggensee 2001; Harms and Feldmeier 2002; Mosunjac et al. 2003).

In spite of numerous references in the medical literature, female genital schistosomiasis (FGS) has been overlooked and has often been mistaken for a sexually transmitted disease (Attili, Hira, and Dube 1983). The presumption by medical professionals and the local population that the symptoms of FGS were in fact symptoms of sexually transmitted diseases has inhibited women from seeking medical care and contributed to stigmatization of women with FGS symptoms (Feldmeier et al. 1995). Even in regions with prevalence of schistosomiasis exceeding 40 percent of the population, such as on the shores of Lake Victoria, people feel that the infection is a shameful condition. Because of its location in the genital organs, they consider it an STD in spite of its transmission in water and the increasing prevalence with proximity to the lake (Mwanga et al. 2004).

Female genital lesions from schistosomiasis bleed spontaneously and from contact. In young girls, lesions are generally located in the vulva and vagina. At sexual maturity, the lesions become more numerous and cluster in the cervix, which is the area most vulnerable to HIV infection in young women (Marble and Key 1995). Genital schistosomiasis promotes the transmission of HIV not only through the general effect of parasite load on nutritional balance and immune activation but also through its direct effect on the immune system barriers (skin and mucosa) and on the cell-mediated response. The numerous lesions produced by the eggs of the schistosome worm on the cervix, the vulva, and the vagina provide direct access to the bloodstream for the HIV virus (Feldmeier et al. 1995). Both viable and dead ova also produce an inflammatory reaction in the tissue and attract $CD4^+$ T cells, which are HIV-susceptible (Poggensee et al. 2000; Mosunjac et al. 2003), to those sites. FGS lesions and inflammation can promote both male-to-female and female-to-male transmission of HIV.

HIV is more prevalent in areas with high schistosome prevalence than in low-prevalence areas (Feldmeier et al. 1995; Marble and Key 1995). Much has been made of the role of commerce in facilitating HIV transmission in Kenya, Uganda, and Tanzania in the regions around Lake Victoria. The emphasis has been on sexual partner change that might accompany the trade in goods across the lake. But the extremely high prevalence of schistosomiasis in the area around the lake has been virtually ignored except by tropical disease specialists.

Genital schistosomiasis in men has been less studied, but there are also indications that it can promote HIV transmission through inflammation of the genital area. In one study in Madagascar, 43 percent of semen samples of a cross-sectional community-based study showed the presence of schistosome eggs. Bleeding associated with male genital schistosome infection is less often noticed than with urinary

schistosomiasis, and so the genital form has been overlooked. In HIV-infected men, such bleeding also promotes viral shedding (Feldmeier et al. 1999; Leutscher et al. 2000). In Africa alone, 200 million people, men and women, are afflicted with genitourinary schistosomiasis (Feldmeier et al. 1999), constituting a very large population with increased susceptibility to HIV or more virulent infections of HIV.

In the HIV literature and in global AIDS policy, there is a great deal of attention paid to the notion of risk behaviors. It is clear from the data we have about schistosomiasis and other parasites that one of the riskiest activities in Africa is to be a little girl or boy who gathers water for the family in a slow-moving stream or helps with the family laundry at creekside or bathes or plays in fresh water. When he or she grows up, that child will have a much higher risk of sexual transmission or acquisition of HIV because of a schistosome infection than a healthy person with similar sexual behavior. AIDS policy needs to address the mundane risks of growing up in Sub-Saharan Africa, Asia, and Latin America that burden people with sickness and make them more vulnerable to HIV.

The connection between parasite infection and HIV transmission makes treatment of schistosomiasis and other parasites a very high priority in an HIV-prevention program (Wolday et al. 2002). Effective treatment for schistosomiasis can be delivered for less than 25 U.S. cents per adult and even less for children (WHO 1996/2003). Treatment, however, provides only temporary relief unless there are also parallel improvements in better water, sanitation, and health education. The demonstration that parasite infection interacts with HIV viral load and HIV transmission makes a recalculation of the cost-effectiveness of eradication of *Schistosoma* and other parasites even more urgent. Eradication through water and sanitation investments is also attractive because once high-cost environmental measures are in place, they generate relatively low recurrent cost (Chandiwana and Taylor 1990).

Conclusion

The same conditions that promote high prevalence of other infectious diseases and parasites are responsible for the spread of the AIDS epidemic in poor populations. Programs to prevent HIV transmission will be unsuccessful unless they address the underlying causes of the spread of AIDS. HIV prevention must be based on scientific evidence regarding cofactor conditions, not, as they currently are, on unproven assumptions about the primacy of behavioral factors. Poverty eradication is ultimately the most important means for stopping AIDS epidemics. Investments in food security, sanitary infrastructure, and education are integral parts of a program of poverty eradication. Food security, deworming, schistosomiasis prevention and treatment, and malaria control programs must be incorporated into HIV prevention.

Inexpensive means and organizational support are already available for achieving these goals and can be integrated with AIDS programming.

For 25 years, global AIDS policy has been divorced from the accumulated knowledge and experience in the field of public health. The limited menu of AIDS interventions evidences little understanding of this complex epidemic. Global health policy is trammeled by reliance on tools of epidemiology and health economics that are too rudimentary to understand a complex epidemic. (For a longer analysis of the limitations of methodology, see Stillwaggon 2006.) Randomized controlled trials and cost-effectiveness studies are useful when the relationships to be studied are simple and easily isolated. Public health problems of populations in poverty are interrelated and synergistic. Furthermore, those conditions may be nearly ubiquitous in poor populations. Attempts to isolate the effects of vitamin A or malaria or worms on HIV transmission may be confounded by other endemic conditions. Treatment of only one condition may not produce measurable results because of the persistent impact of other maladies. Global AIDS policy is paralyzed because epidemiologic methods demand a "smoking gun" as evidence of relationships between HIV and the endemic conditions of malnutrition, parasites, and infectious disease. Such a burden of proof is inappropriate because interventions to reduce malnutrition, parasite load, and infectious diseases are beneficial in themselves and because a century of health research has demonstrated that they are necessary to prevent new epidemics, such as HIV/AIDS.

References

Attili, V. R., S. Hira, and M. K. Dube. 1983. Schistosomal genital granulomas: a report of 10 cases. *British Journal of Venereal Disease* 59: 269–272.

Beisel, W. 1996. Nutrition and immune function: Overview. *Journal of Nutrition* 126: 2611S–2615S.

Bentwich, Z., A. Kalinkovich, Z. Weisman, G. Borkow, N. Beyers, and A. Beyers. 1999. Can eradication of helminthic infections change the face of AIDS and tuberculosis? *Immunology Today* 20 (11): 485–487.

Borkow, G., Q. Leng, Z. Weisman, M. Stein, N. Galai, A. Kalinkovich, and Z. Bentwich. 2000. Chronic immune activation associated with intestinal helminth infections results in impaired signal transduction and anergy. *The Journal of Clinical Investigation* 106 (8): 1053–1060.

Borkow, G., Z. Weisman, Q. Leng, M. Stein, A. Kalinkovich, D. Wolday, and Z. Bentwich. 2001. Helminths, human immunodeficiency virus and tuberculosis. *Scandinavian Journal of Infectious Disease* 33: 568–571.

Chandiwana, S., and P. Taylor. 1990. The rational use of antischistosomal drugs in schistosomiasis control. *Social Science and Medicine* 30 (10): 1131–1138.

Chandra, R. K. 1997. Nutrition and the immune system: An introduction. *American Journal of Clinical Nutrition* 66: 460S–463S.

Corbett, E., R. Steketee, F. ter Kuile, A. Latif, A. Kamali, and R. Hayes. 2002. HIV-1/AIDS and the control of other infectious diseases in Africa. *Lancet* 359: 2177–2187.

Cunningham-Rundles, S. 1998. Analytical methods for evaluation of immune response in nutrient intervention. *Nutrition Reviews* 56 (1, Part 2): S27–S37.

Fawzi, W. W., and D. J. Hunter. 1998. Vitamins in HIV disease progression and vertical transmission. *Epidemiology* 9 (4): 457–466.

Fawzi, W. W., G. I. Msamanga, D. Spiegelman, E. Urassa, N. McGrath, D. Mwakagile, G. Antelman, R. Mbise, G. Herrera, S. Kapiga, W. Willett, and D. Hunter. 1998. Randomised trial of effects of vitamin supplements on pregnancy outcomes and T cell counts in HIV-1-infected women in Tanzania. *Lancet* 351: 1477–1482.

Feldmeier, H., G. Helling-Giese, and G. Poggensee. 2001. Unreliability of PAP smears to diagnose female genital schistosomiasis. *Tropical Medicine and International Health* 6 (1): 31–33.

Feldmeier, H., P. Leutscher, G. Poggensee, and G. Harms. 1999. Male genital schistosomiasis and haemospermia. *Tropical Medicine and International Health* 4 (12): 791–793.

Feldmeier, H., G. Poggensee, I. Krantz, and G. Helling-Giese. 1995. Female genital schistosomiasis. *Tropical and Geographical Medicine* 47 (2, Supplement): 2–15.

Friedman, J., J. Kurtis, R. Mtalib, M. Opollo, D. Lanar, and P. Duffy. 2003. Malaria is related to decreased nutritional status among male adolescents and adults in the setting of intense perennial transmission. *The Journal of Infectious Diseases* 188: 449–457.

Friis, H., and K. F. Michaelsen. 1998. Micronutrients and HIV infection: A review. *European Journal of Clinical Nutrition* 52: 157–163.

Gopinath, R., M. Ostrowski, S. Justement, A. Fauci, and T. Nutman. 2000. Filarial infections increase susceptibility to human immunodeficiency virus infection in peripheral blood mononuclear cells in vitro. *Journal of Infectious Diseases* 182 (6): 1804–1808.

Harms, G., and H. Feldmeier. 2002. Review: HIV infection and tropical parasitic diseases—deleterious interactions in both directions? *Tropical Medicine and International Health* 7 (6): 479–488.

Hedberg, K., N. Shaffer, F. Davachi, A. Hightower, B. Lyamba, K. Paluki, P. Nguyen-Dinh, and J. Breman. 1993. *Plasmodium falciparum*-associated anemia in children at a large urban hospital in Zaire. *American Journal of Tropical Medicine and Hygiene* 48 (3): 365–371.

Hoffman, I., C. Jere, T. Taylor, P. Munthali, J. Dyer, J. Wirima, S. Rogerson, N. Kumwenda, J. Eron, S. Fiscus, H. Chakraborty, T. Taha, M. Cohen, and M. Molyneux. 1999. The effect of *Plasmodium falciparum* malaria on HIV-1 RNA blood plasma concentration. *AIDS* 13: 487–494.

John, G., R. Nduati, D. Mbori-Ngacha, J. Overbaugh, M. Welch, B. Richardson, J. Ndinya-Achola, J. Bwayo, J. Krieger, F. Onyango, and J. Kreiss. 1997. Genital shedding of human immunodeficiency virus type 1 DNA during pregnancy: Association with immunosuppression, abnormal cervical or vaginal discharge, and severe vitamin A deficiency. *The Journal of Infectious Diseases* 175: 57–62.

Khandait, D. W., N. D. Vasudeo, S. Zodpey, D. Kumbhalkar, and M. Koram. 1998. Subclinical vitamin A deficiency in undersix children in Nagpur, India. *Southeast Asian Journal of Tropical Medicine and Public Health* 29 (2): 289–292.

Landers, D. 1996. Nutrition and immune function II: Maternal factors influencing transmission. *Journal of Nutrition* 126: 2637S–2640S.

Leutscher, P., C.-E. Ramarokoto, C. Reimert, H. Feldmeier, P. Esterre, and B. Vennervald. 2000. Community-based study of genital schistosomiasis in men from Madagascar. *The Lancet* 3555: 117–118.

Marble, M., and K. Key. 1995. Clinical facets of a disease neglected too long. *AIDS Weekly Plus* August 7: 16–19.

McMurray, D. 1998. Impact of nutritional deficiencies on resistance to experimental pulmonary tuberculosis. *Nutrition Reviews* 56 (1, Part 2): S147—S152.

Mosunjac, M., T. Tadros, R. Beach, and B. Majmudar. 2003. Cervical schistosomiasis, human papilloma virus (HPV), and human immunodeficiency virus (HIV): A dangerous coexistence or coincidence? *Gynecologic Oncolgy* 90 (1): 211–214.

Mwanga, J. R., P. Magnussen, C. Mugashe, R. Gabone, and J. Aagaard-Hansen. 2004. Schistosomiasis-related perceptions, attitudes and treatment-seeking practices in Magu District, Tanazania: Public health implications. *Journal of Biosocial Science* 36: 63–81.

Nimmagadda, A., W. O'Brien, and M. Goetz. 1998. The significance of vitamin A and carotenoid status in persons infected by the human immunodeficiency virus. *Clinical Infectious Diseases* 26: 711–718.

Poggensee, G., I. Kiwelu, V. Weger, D. Göppner, T. Diedrich, I. Krantz, and H. Feldmeier. 2000. Female genital schistosomiasis of the lower genital tract: prevalence and disease-associated morbidity in northern Tanzania. *The Journal of Infectious Diseases* 181: 1210–1213.

PPC (Partnership for Parasite Control). 2002. Rome meeting notes, 2002. http://www.who.int/wormcontrol/about_us/en/mtgnotes/april2002.pdf.

Rowland-Jones, S., and B. Lohman. 2002. Interactions between malaria and HIV infection—an emerging public health problem? *Microbes and Infection* 4: 1265–1270.

Ruel, T., J. A. Rivera, M. Santizo, B. Lönnerdal, and K. Brown. 1997. Impact of zinc supplementation on morbidity from diarrhea and respiratory infections among rural Guatemalan children. *Pediatrics* 99 (6): 808–813.

Scrimshaw, N., and J. P. SanGiovanni. 1997. Synergism of nutrition, infection, and immunity: An overview. *American Journal of Clinical Nutrition* 66: 464S–477S.

Semba, R. 1998. The role of vitamin A and related retinoids in immune function. *Nutrition Reviews* 56 (1, Part 2): S38–S48.

Semba, R., P. Miotti, J. Chiphangwi, A. Saah, J. Canner, G. Dallabetta, and D. Hoover. 1994. Maternal vitamin A deficiency and mother-to-child transmission of HIV-1. *Lancet* 343: 1593–1597.

Shankar, A. H., B. Genton, R. Demba, M. Baisor, J. Paino, S. Tamja, T. Adiguma, L. Wu, L. Rare, J. Tielsch, M. Alpers, and K. West Jr. 1999. Effect of vitamin A supplementation on morbidity due to *Plasmodium falciparum* in young children in Papua New Guinea: A randomised trial. *Lancet* 354: 203–209.

Sharp, D. 2003. Dam medicine. *The Lancet* 362: 184.

Solomons, N. 1998. Plant sources of vitamin A and human nutrition: Red palm oil does the job. *Nutrition Reviews* 56 (10): 309–311.

Sommer, A., K. West, K. West, and A. Ross. 1996. *Vitamin A deficiency: health, survival, and vision.* New York: Oxford University Press.

Stephensen, C. B., J. O. Alvarez, J. Kohatsu, R. Hardmeier, J. Kennedy Jr., and R. Gammon Jr. 1994. Vitamin A is excreted in the urine during acute infection. *American Journal of Clinical Nutrition* 60 (3): 388–392.

Stillwaggon, E. 2006. *AIDS and the ecology of poverty.* New York: Oxford University Press.

Whitworth, J., D. Morgan, M. Quigley, A. Smith, B. Mayanja, H. Eotu, N. Omoding, M. Okongo, S. Malamba, and A. Ojwiya. 2000. Effect of HIV-1 and increasing immunosuppression on malaria parasitaemia and clinical episodes in adults in rural Uganda: A cohort study. *Lancet* 356: 1051–1056.

WHO (World Health Organization). 1996 last updated/2003. *Schistosomiasis.* Fact Sheet No. 115, http://www.who.int/inf-fs/en/fact115.html.

Wolday, D., S. Mayaan, Z. Mariam, N. Berhe, T. Seboxa, S. Britton, N. Galai, A. Landai, and Z. Bentwich. 2002. Treatment of intestinal worms is associated with decreased HIV plasma viral load. *Journal of Acquired Immune Deficiency Syndromes* 31: 56–62.

Woodward, B. 1998. Protein, calories, and immune defenses. *Nutrition Reviews* 56 (1, Part 2): S84–S92.

World Bank. 1997. *Confronting AIDS: Public priorities in a global epidemic.* Oxford: Oxford University Press.