HIV/AIDS AND NUTRITION

A Review of the Literature and Recommendations for Nutritional Care and Support in Sub-Saharan Africa

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SARA
USAID

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Acronyms and Abbreviations

ACC/SCN	Administrative Committee on Coordination Sub-Committee on Nutrition
AED	Academy for Educational Development
AIDS	acquired immunodeficiency syndrome
ARV	antiretroviral
BCM	body cell mass
CRHCS	Commonwealth Regional Health Community Secretariat
FAO	Food and Agriculture Organization
GI	gastrointestinal
GLN	glutamine
HIV	human immunodeficiency virus
IgM	immunoglobulin M
IMCI	Integrated Management of Childhood Illness
MTCT	mother-to-child transmission (of HIV)
NAIDS	nutritionally acquired immune deficiency syndrome
NVP	nevirapine
PCR	polymerase chain reaction
PLWHA	people living with HIV/AIDS
RDA	recommended daily allowance
RNA	ribonucleic acid
SARA	Support for Analysis and Research in Africa
SLPI	secretory leukocyte protease inhibitor
SP	Sulfadoxine pyrimethamine
TB	tuberculosis
TNF	tumor necrosis factor
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
VCT	voluntary counseling and testing
ZDV	zidovudine (also, azidothymadine, AZT)

Executive Summary

The HIV/AIDS epidemic continues to have a devastating effect on sub-Saharan Africa. By the end of 1998, at least 34 million people living in sub-Saharan Africa had become infected with HIV, and some 11.5 million of these have already died. In 1998 alone, about 2 million Africans died from HIV/AIDS. The AIDS epidemic in Africa has created unprecedented morbidity and mortality in young adults, reduced life expectancy, and diverted scarce resources from other pressing development problems. The toll the epidemic has taken on women and children is particularly acute.

Malnutrition has been an endemic problem in Africa for decades, complicated by a combination of factors, and more recently, by the impact of AIDS. It is estimated that about one-third of all children under 5 in sub-Saharan Africa are stunted and more than half suffer from some form of micronutrient malnutrition. Malnutrition is also common among adults in Africa, where more than half of all pregnant women suffer from anemia and much of the population is at risk for iodine deficiency.

HIV/AIDS and malnutrition are inextricably interrelated. Research suggests that malnutrition increases the risk of HIV transmission from mothers to babies and the progression of HIV infection. In turn, HIV infection exacerbates malnutrition through its attacks on the immune system and its impact on nutrient intake, absorption, and utilization. Malnutrition also increases fatigue, and it decreases physical activity and work productivity of people living with HIV and AIDS (PLWHA).

This paper informs health professionals working in nutrition and/or health programs about of the role of nutrition in HIV infection in African settings, and describes three overlapping processes that lead to weight loss and wasting in PLWHA: reductions in food intake, nutrient malabsorption, and metabolic alterations. Several vitamins and minerals are critical for fighting HIV because they are required by the immune system and major organs to fight infectious pathogens. The paper explores what is known about the possible effects of these nutrients on HIV disease progression and mortality, and on mother-to-child transmission of HIV.

The paper reviews research that indicates that in the early period of HIV infection, weight gain and/or maintenance might be achieved, and it addresses the extent to which nutrition counseling and interventions can slow or reverse the process and consequences of weight loss and wasting in PLWHA. It presents examples of a number of nutrition support programs, ranging from offering nutrition guidelines and dietary advice, to offering palliative and home-based care, to provision of food, that are being offered to PLWHA in Africa.

The paper provides evidence-based, practical nutrition care and support recommendations for four categories of PLWHA in Africa: asymptomatic individuals; individuals who are experiencing weight loss; adults with AIDS; and children suffering from HIV and AIDS. Guidelines for the development of programs to provide nutritional care and support for PLWHA in Africa are also provided.

Existing data suggest that nutrition interventions to increase energy and protein intakes of people living with HIV may help to build their reserves and reduce their vulnerability to weight loss and wasting that accompanies diarrhea and other opportunistic infections. Improvements in micronutrient intake and status may also help to strengthen the immune system, to reduce the adverse consequences of infection-related oxidative stress, and to lengthen survival. Both interventions may help people living with HIV to remain relatively healthy, prolonging the interval from initial infection to development of AIDS and improving the quality of their lives. At later stages of the disease, nutrition support is largely palliative and focused on the dietary management of conditions that affect appetite, digestion, and comfort when

eating. These interventions are focused primarily on maintaining intake during bouts of illness and recuperative feeding when acute symptoms subside.

The fact that HIV can be transmitted from HIV-infected mothers to their infants through breastfeeding focuses on attention on one of the most obvious and difficult relationships between HIV and nutrition. The paper explores the complexities of weighing the competing risks of HIV transmission through breastfeeding with the various risks of replacement feeding. Recent research on HIV and breastfeeding is reviewed, and recommendations for safer breastfeeding are made.

The paper concludes with recommendations for further research in the fields of nutritional management of HIV/AIDS and reduction of the risk of mother-to-child transmission of HIV.

Introduction

Providing sufficient food and nutrition to meet people's basic needs for health, growth and development has been a long-standing challenge for African countries. This challenge is further exacerbated by the emergence of HIV/AIDS. At a national and family level, the HIV epidemic has weakened societies and economic status in Africa, making it even more difficult to ensure food security, education, and other basic services. It has dramatically increased morbidity and mortality in infants, children, and adults. On a personal level, HIV contributes to malnutrition for physiological reasons related to the infection itself and because people living with HIV and AIDS (PLWHA) often have diets that are deficient in energy, protein, vitamins, and other nutrients.

The relationship between malnutrition and AIDS is well recognized. In fact, in Africa AIDS was initially known as "Slim Disease" because of the classic wasting syndrome typically experienced by persons with the disease. HIV infection compromises the nutritional status of infected individuals and, in turn, poor nutritional status can affect the progression of HIV infection. In recent years, considerable progress has been made both in understanding the biological mechanisms responsible for these relationships, and in beginning to identify nutritional interventions that may improve the quality and length of life for people living with HIV. Much of this work comes from Africa, the region hardest hit by the AIDS epidemic.

In spite of this progress, there are still many gaps in our understanding of the relationship between HIV/AIDS and nutrition, and health providers still lack practical, evidence-based advice on appropriate nutrition for PLWHA. It is still unclear whether, to what extent, and how nutrition therapy or supplementation might positively affect HIV-infected individuals. Finding effective, affordable, and acceptable nutritional interventions for PLWHA is especially important in Africa today because many of the new advances in AIDS treatment available in industrialized countries, such as highly active antiretroviral (ARV) therapies, will remain unaffordable for most Africans affected by the disease for the foreseeable future.

The first regional workshop in Africa on HIV and Nutrition was organized by the Food and Nutrition Programme of the Commonwealth Regional Health Community Secretariat (CRHCS) and held in Maputo, Mozambique, in February 1999. In keeping with the recommendations that emerged from this workshop, CRHCS requested the Support for Analysis and Research in Africa (SARA) Project of the Academy for Educational Development (AED) to prepare this paper on HIV and nutrition.

The objectives of this paper are to:

- review what is known about the clinical and social dimensions of HIV and nutrition relationships, as relevant to the African context;
- synthesize current understanding of the role of macronutrients and micronutrients in HIV infection, as relevant in African settings;
- describe the impact of HIV on nutritional status and the impact of nutritional status on HIV progression and transmission, including mother-to-child transmission (MTCT) of HIV;
- highlight important research and program experience from Africa; and
- identify research gaps and make recommendations for programs addressing HIV and nutrition.

Several papers reviewing the literature on HIV/AIDS and nutrition have been published recently (e.g., Babameto and Kotler, 1997; Baum and Shor-Posner, 1998; Fawzi and Hunter, 1998; Friis and Michaelson, 1998; Tang and Smit, 1998; Semba and Tang, 1999). This paper will complement these excellent and comprehensive reviews by summarizing research issues and findings, and by focusing on practical, programmatic responses to the intersecting problems of HIV/AIDS and malnutrition in Africa.

I. HIV/AIDS[1]

A. Epidemiology and Social Impact

Africa is the global epicenter of AIDS. An estimated 83 percent of all of the world's AIDS deaths, since the start of the epidemic, occurred in Africa. By the end of 1998, at least 34 million people living in sub-Saharan Africa had become infected with HIV, and some 11.5 million of these have already died. In 1998 alone, about 2 million Africans died from HIV/AIDS (UNAIDS, 1999).

Countries in the southern and eastern parts of Africa are particularly affected. In Botswana, Namibia, Swaziland, and Zimbabwe, for example, between 20 percent and 26 percent of adults aged 15-49 are HIV-infected. In other countries, such as Central African Republic, Cote d'Ivoire, Kenya, Tanzania, and Uganda, at least 10 percent of adults are HIV-infected. Overall, about 65 percent of all new adult HIV infections occur in young men and women less than 30 years old (UNAIDS, 1999). For a map of HIV-1 infection levels in low-risk urban populations of Africa, see **Figure 1**.

To present the magnitude of the impact of HIV/AIDS in Africa another way, Van de Perre (1999) estimates that there are three times more children living with HIV in the city of Bobo-Dioulasso, Burkina Faso (400,000 inhabitants), than in the entire country of France (58 million inhabitants).

Women in Africa, especially young women, are disproportionately affected by HIV/AIDS. Data suggest that about 55 percent of all new infections in Africa occur among women and, as of the end of 1999, the number of infected women has surpassed the number of infected men by more than 2 million. Recent studies show that women 15-19 years of age are five to six times more likely to be HIV-infected than men in the same age group (UNAIDS, 2000).

Children are not exempt from the direct and indirect effects of AIDS either. High birth rates and high rates of HIV infection in African women contribute to large numbers of infants infected with HIV and rapidly increasing infant and child mortality due to pediatric AIDS-related deaths (Connolly et al, 1998). In Harare, Zimbabwe, for example, infant mortality is estimated to have increased from 30 to 60 per 1,000 live births between 1990 and 1996 and the child mortality rate rose from 8 to 20 per 1000 live births in the same period (UNAIDS, 1999). Across AIDS-affected Africa, the epidemic is reversing the gains made in child survival through measures such as promotion of breastfeeding, immunization, and use of oral rehydration therapy.

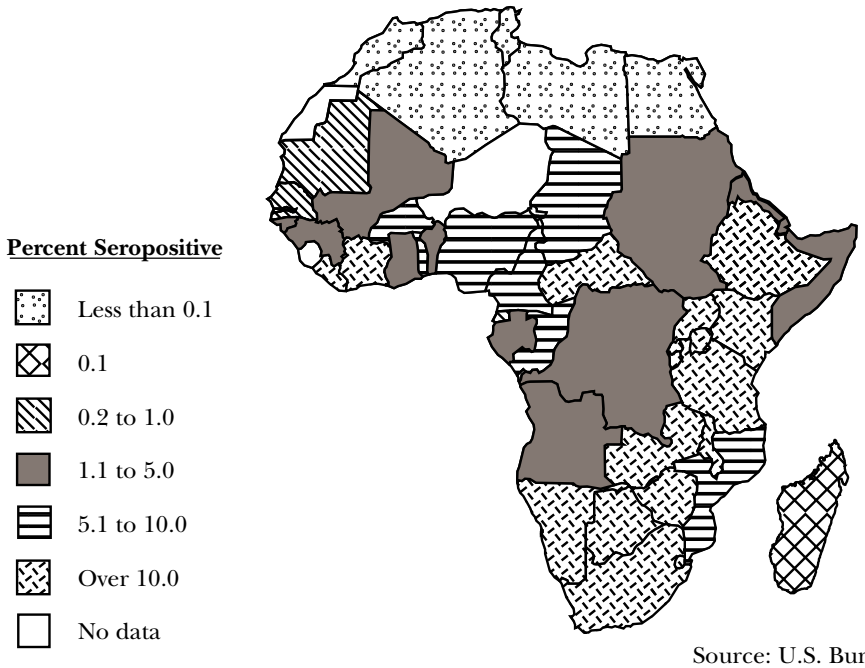
The role that breastfeeding plays in mother-to-child transmission of HIV illustrates one important link between HIV and nutrition. Breastfeeding is a tradition in Africa, and breastmilk is the main source of nutrition for infants during their first years of life. In addition, breastfeeding provides psychological and child-spacing benefits to infants and mothers, and reduces infant and child morbidity and mortality by protecting children from diarrheal diseases, pneumonia, and other infections. Unfortunately, between 10 and 20 percent of HIV-infected mothers will pass the virus to their babies through extended breastfeeding.

Adult mortality is also severely affected by AIDS in Africa and the epidemic is responsible for declining life expectancy and changing population structures in many countries. In parts of East Africa, for example, where HIV infection rates are around 10 percent, HIV more than doubles the probability of dying at an early age (UNAIDS, 1999). Life expectancy has already decreased by 20 to 40 percent in countries such as South Africa, Uganda, Kenya, Zambia, Zimbabwe, and Botswana (UNAIDS, 2000). The epidemic will eventually create a population 'chimney' in these hard-hit countries, with relatively few persons older than 40 years remaining alive to care for the young and the elderly (UNAIDS, 2000).

The socioeconomic impact of the AIDS epidemic in African countries that are already struggling with conditions of extreme poverty has been disastrous. At the national level, costs of HIV prevention and treatment of AIDS have diverted scarce resources

[1] All references to HIV in this paper refer to HIV-1.

FIGURE 1. African HIV-1 Seroprevalence for Low-Risk Urban Populations



Source: U.S. Bureau of the Census (2000)

from other development efforts, including efforts to promote food security, improve health services, and increase education and economic productivity. At the family level, illness and death from AIDS have profoundly affected family well being, including caregivers' ability to ensure adequate food and nutrition for the family. AIDS orphans in Africa have become a growing and highly vulnerable group. An estimated 12 million African children have already lost their mother or both parents to AIDS before age 15 and the number of AIDS orphans is expected to grow dramatically in the next 10 years (UNAIDS, 2000).

B. HIV/AIDS in Adults

In Africa, HIV transmission in adults occurs most commonly through sexual intercourse. After transmission, HIV infection generally follows a common pattern in all regions of the world, although the interval between phases may be shorter in developing than in industrialized countries (Bartlett and Finkbeiner, 1998). These phases are:

1. **Acute infection:** HIV causes symptoms of acute infection (such as fever and body ache) that clear up spontaneously, generally within 1 to 6 weeks after infection. Concentration of the virus in the blood, also known as viral load, is high at this time. If a woman is pregnant or breastfeeding at the time of infection, the risk of MTCT of HIV is greater due to the high viral load. Although symptoms of acute infection may be experienced, the body has not yet produced antibodies to the virus and standard HIV antibody tests will be negative. This phase of infection usually lasts between 1 and 3 weeks.

2. **Seroconversion:** An individual undergoes seroconversion when the body begins to produce antibodies to HIV. Seroconversion generally takes place 6 to 12 weeks after HIV infection. HIV antibodies can be measured through a blood test; a positive antibody test confirms that adults are HIV infected. However, infants born to HIV-infected mothers still carry their mother's antibodies, even if the infants themselves are not infected. These maternal antibodies may remain in their bodies for 12 to 15 months. For this reason, standard HIV antibody tests cannot confirm HIV infection in infants younger than 12 to 15 months of age.

3. **Asymptomatic period:** In most cases there is usually a prolonged period (several years) when an infected person feels well and has no symptoms of infection. During this period, the

infected individual's immune system is gradually affected by the disease and CD4 T-lymphocyte cell counts gradually decline. The effect of HIV on nutrition begins during this asymptomatic period.

4. **Early symptomatic infection:** During this period, the first symptoms of a weakened immune system occur. Common conditions include fungal infections of the mouth and other mucosal surfaces (e.g., oral thrush), shingles, excessive bruising and bleeding, bacterial (pneumococcal) pneumonia, tuberculosis, chronic fatigue, fever, weight loss, and chronic diarrhea. These conditions tend to persist for several weeks or months in people living with HIV.

5. **Late symptomatic infection:** This stage officially constitutes the condition called AIDS and it is defined by a blood test that confirms a low number of immune cells (i.e., CD4 T-lymphocyte cell counts < 200) or by the presence of various other severe complications. HIV viral load is high during this stage because the immune system is not able to control the infection. As the viral load increases, the risk of transmission to others also increases.

In industrialized countries, the average length of time between HIV infection and AIDS diagnosis is 8 to 10 years. In developing countries, this time period and the time between AIDS diagnosis and death may be shortened by exposure to pathogens and infectious diseases, poor health care, and malnutrition (Grant et al, 1997; Morgan et al, 1997; Greenberg et al, 1998).

Table 1 contains a description of HIV diagnostic tests and their applications.

TABLE 1. Tests to Diagnose HIV and to Measure Its Progression

HIV antibody tests	These tests (initially performed with blood samples but now also with saliva samples) measure the presence of antibodies to HIV, and include HIV ELISA, immunofluorescence, and western blot assays.
P24 antigen test	This test measures actual HIV virus in the blood, and is a useful measure of infection during the period before which the body has developed measurable antibodies to HIV.
Virologic assays	These tests include HIV DNA Polymerase Chain Reaction (PCR) and HIV RNA detection methods and culture. These tests are especially useful in defining or ruling out HIV infection in infants less than 18 months of age. (Antibody tests cannot be reliably used in infants, since they cannot differentiate between the infant's own HIV antibodies and transplacentally-acquired maternal antibodies).
CD4 cell count	CD4 cells are also referred to as T4 cell and T-helper cells. CD4 cell count is measured from blood samples. CD4 cell count measures the number of CD4 cells, which are critical to the immune system's functioning, and that are infected and destroyed by HIV. This test measures the state of the immune system and its rate of deterioration. The higher the CD4 cell count, the better the individual's condition and prognosis. The following levels of CD4 cell counts indicate the various conditions: 500-1400: average counts in healthy, HIV-negative individuals <500: immune system is damaged <35: damage is moderately severe <200: damage is severe and the patient is officially diagnosed as having AIDS <50: disease is advanced and damage may be irreparable The CD4 cell count and viral load test are often used in a complementary fashion for clinical purposes.
Viral load test	The HIV virus has been found, and, for research purposes, measured in many body fluids including blood, saliva, breastmilk, semen and vaginal secretions. For clinical purposes, the viral load test measures the number of viruses in one milliliter of blood and is reported as "copies per milliliter." Viral load can measure the rapidity with which HIV disease is progressing—the higher the viral load, the faster and more severe the progression.

Adapted from Bartlett and Finkbeiner (1998), Nielsen and Bryson (2000) and Roitt et al (1998).

C. Pediatric HIV/AIDS

Infants can acquire HIV from their infected mothers during pregnancy, at the time of delivery, or after birth through breastfeeding. Although less common, infants may also become infected with HIV from contact with infected blood or blood products or HIV-contaminated medical equipment.

In the absence of interventions to prevent mother-to-child transmission, studies suggest that between 25 and 45 percent of HIV-infected breastfeeding women pass on the virus to their babies. About 20 percent of this transmission takes place during pregnancy, and the remaining 80 percent of MTCT occurs during delivery (40 percent) and through extended breastfeeding—up to 24 months (40 percent). Put another way, 5 to 10 percent of HIV-infected women will pass the virus to their babies during a pregnancy; 10 to 20 percent will pass the virus during delivery; and another 10 to 20 percent will pass the virus over the course of 2 years of breastfeeding (De Cock et al, 2000; Dunn et al, 1992). Additional information on HIV transmission through breastfeeding is found in Chapter V.

The clinical presentation of pediatric AIDS has been documented in several African countries. The most common features of pediatric HIV are pulmonary infections (including pneumonia and tuberculosis), persistent diarrhea, growth failure, swollen lymph nodes, chronic cough, and chronic fever (Lepage et al, 1998). Personnel, facilities, and drugs to treat even common diseases remain scarce in many parts of Africa.

Low birth weight is common in newborns of HIV-infected mothers, resulting in increased perinatal morbidity and mortality. Data from several African countries indicate that low weight-for-age and stunting are greater among HIV-infected children when compared with the general population. However, wasting (low weight-for-height) is believed to be uncommon except among those who are hospitalized or have progressed from HIV to AIDS, and possibly also among those who are not breastfed (Lepage et al, 1996).

Disease progression in children who acquire HIV infection from their mothers is more rapid in Africa than in industrialized countries, probably because African children are exposed to early and multiple infectious, and have high rates of malnutrition and micronutrient deficiencies (Dray-Spira et al, 2000). Studies suggest that about one-quarter to one-third of HIV-infected infants die by 12 months of age, and about one-half to two-thirds die by their fifth birthday (Lepage et al, 1998).

Recently, WHO has updated its clinical approach to diagnosing symptomatic HIV in children living in settings where diagnostic testing is not available, and new management guidelines are being integrated into the Integrated Management of Childhood Illness (IMCI) protocols. According to the new guidelines (WHO, 2000), children presenting with any 3 of the following signs or conditions are suspected to have HIV infection:

- 2 or more chest infections requiring antibiotics (pneumonia) in the past two months;
- 1 or more episode of persistent diarrhea OR 2 or more episodes of acute diarrhea in the past two months;
- a parent with tuberculosis;
- oral candidiasis (thrush);
- enlarged lymph nodes in two or more sites;
- growth faltering (weight curve flat or falling for two consecutive months);
- weight-for-age below the 3rd percentile (using international growth reference standards).

The guidelines suggest that health workers should be given special training in to how to treat children suspected of HIV infection in countries where over 2 percent of the adult population is HIV-infected. This includes managing children who do not respond to standard IMCI treatment protocols, have signs and symptoms of HIV infection, or have an epidemiologic history suggestive of HIV (WHO, 2000; Lepage et al, 1998).

II. Malnutrition

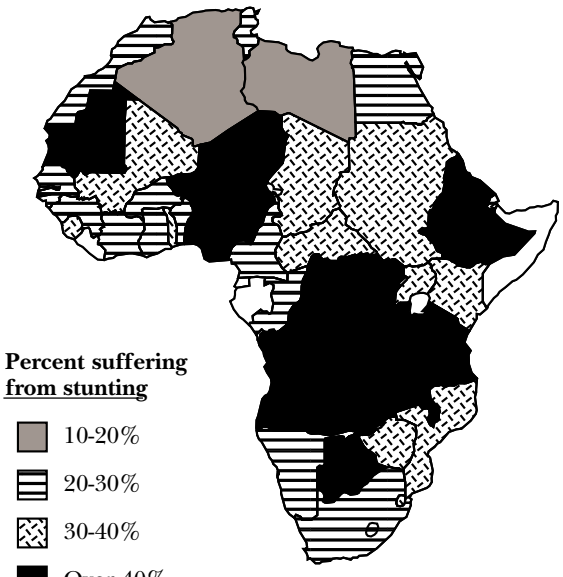
Improving the nutrition situation in Africa has been a challenge for decades, complicated by a combination of individual, household, community, national, and international factors, including, in the last decade, the emergence of AIDS. Disease, cultural beliefs and customs, high fertility rates, poor economic status, and limited access to health and other social services also contribute to chronic, endemic malnutrition in this region (Ndure et al, 1999).

Malnutrition takes many forms. These include protein-energy malnutrition, which is usually measured in terms of body size, and micronutrient malnutrition, which in its mild and moderate forms is not always recognized and is often referred to as "hidden hunger." Common indicators of protein-energy malnutrition are low[2] height-for-age (stunting), low weight-for-age (underweight), and low weight-for-height (also known as wasting or acute malnutrition) in children and low body mass index[3] (BMI) in adults. The most commonly reported micronutrient deficiencies in both children and adults are iron, vitamin A, and iodine deficiency. Deficiencies in other vitamins and minerals that are vital for the body's normal functions, including the work of the immune system, are not commonly measured but frequently occur in populations with high infectious disease burdens and monotonous, poor quality diets characterized by limited consumption of animal products, and seasonal or periodic food insecurity.

In children, nutritional indicators often serve as proxy indicators of their overall well being in developing countries because they reflect the burden of infectious diseases on the community, as well as access to food and caring practices (UNICEF, 1998). Recent data suggest that little or no progress has been made in reducing the prevalence of malnutrition among children in sub-Saharan Africa in the last 20 years, and in several countries, malnutrition is increasing as a result of armed conflicts, deteriorating health systems, shrinking economies, and HIV/AIDS. Much of Africa's child disease burden is directly related to malnutrition (Murray and Lopez, 1996).

The United Nations (UN) currently estimates that about 35 percent of children less than 5 years of age in sub-Saharan Africa are stunted (ACC/SCN, 2000), although country estimates range from around 20 percent in South Africa and Zimbabwe to over 50 percent in Mozambique, Tanzania, and Ethiopia (see **Figure 2**). Around 10 percent of African children suffer from wasting, although, again, there is variation between countries and within age groups, with children under 2 years most severely affected (ACC/SCN, 1997). Vitamin A deficiency is widespread, with countries reporting between 20 and 70 percent of children suffering from sub-clinical deficiency (serum retinol < 0.7 mmol/L). About 60 percent of African children under 5 years suffer from anemia. These forms of malnutrition result in impaired immune systems and inability to fight infection; increased infant and young child mortality; and fatigue, apathy, and reduced cognitive and mental development.

FIGURE 2. Percent of Under-fives (1990-98) Suffering from Stunting, Moderate and Severe



Source: UNICEF (2000)

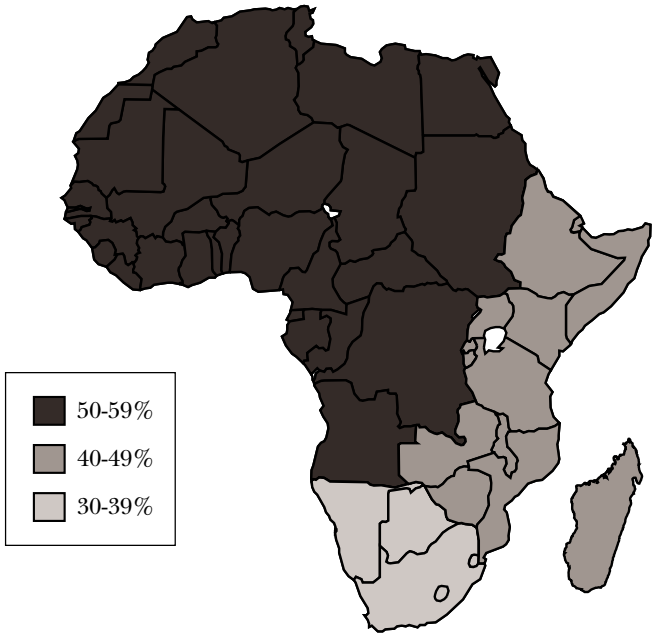
[2] Below -2 standard deviations from the international reference median

[3] Generally expressed as weight/(height^2)

Malnutrition in African adults, and especially among women of childbearing age, is also a serious problem, with an estimated 42 percent of African women as a whole, and half of pregnant women, suffering from anemia (see **Figure 3**). Between 10 and 20 percent of African women 20 to 49 years of age are underweight and nearly 50 percent of the African population is at risk of iodine deficiency disease (ACC/SCN, 2000). Consequences of malnutrition in women of reproductive age include increased risk of complications during pregnancy, adverse pregnancy outcomes, and acquisition of some kinds of infections, as well as reduced work productivity (Baker et al, 1996).

Readers interested in a more detailed description of malnutrition in Africa and its consequences for health, education, food security, and economic productivity are referred to ACC/SCN (2000), Kean et al (1999), and UNICEF (1998).

FIGURE 3. Prevalence of Anemia (hemoglobin < 11 g/dl) in Pregnant African Women



Source: WHO (1992)

III. The Relationship Between HIV/AIDS and Malnutrition

The relationship between HIV/AIDS and malnutrition presents a classic example of the well-recognized "vicious cycle" of immune dysfunction, infectious disease, and malnutrition. Changes in the immune function due to malnutrition are strikingly similar to those induced by HIV/AIDS. In fact, for many years, the impairment to immune function caused by malnutrition has been referred to as the "Nutritionally Acquired Immune Deficiency Syndrome," or NAIDS.

Recent research, much of it conducted in Africa, has shown that nutritional status may affect the progression of HIV disease in adults and the survival of HIV-infected individuals. Malnutrition associated with HIV/AIDS is known to be the result of several processes, but the degree to which nutrition therapy can positively alter the course of HIV disease among PLWHA in Africa is largely unknown.

In this chapter, the clinical and social contexts of HIV/AIDS and malnutrition are summarized. What is known about the roles of macronutrients and micronutrients in HIV/AIDS is described. Issues to consider when interpreting the literature on HIV/AIDS and nutrition are also discussed.

A. The Clinical Context

Long before the AIDS epidemic emerged in Africa in the early 1980s, the synergistic interactions between infection, nutritional status, and immune function were recognized. Infectious diseases, no matter how mild, influence nutritional status, and conversely, almost any nutrient deficiency, if sufficiently severe, will impair resistance to infection (Scrimshaw and SanGiovanni, 1997). This section will first discuss HIV/AIDS and the immune system in general; and then will review the specific relationship between HIV/AIDS, the immune system, and nutritional status.

All environments contain infectious microbes, including viruses, bacteria, and fungi, and these are often more prevalent in Africa than in industrialized countries. These microbes cause disease which, if unchecked, can lead to death. In healthy individuals, the immune system protects the individual from damage by these microbes. People with HIV and AIDS, whose immune systems are compromised, have difficulty resisting a variety of serious infections and conditions.

Viruses (such as HIV) act by replicating inside host cells. To eliminate the infection, the immune system must recognize and destroy these infected cells. The cells that mediate immunity include lymphocytes. Among the lymphocytes, CD4 cells (also called T4 cells and T-helper cells) are critical to the immune system's functioning. HIV infection destroys CD4 cells and leads to a deterioration of the overall immune system. HIV also infects cells of the intestine, brain, and other body organs. Its pervasive nature has made control of HIV infection challenging for clinicians who treat PLWHA and for researchers who are trying to develop effective therapies and vaccines to control the virus.

Infections affect nutritional status by reducing dietary intake and nutrient absorption, and by increasing the utilization and excretion of protein and micronutrients as the body mounts its "acute phase response" to invading pathogens. Anorexia, fever, and catabolism of muscle tissue frequently accompany the acute phase response. Infections also result in the release of pro-oxidant cytokines and other reactive oxygen species. This leads to the increased utilization of "antioxidant" vitamins (e.g., vitamin E, vitamin C, beta-carotene) as well as the sequestration of several minerals (e.g., iron, zinc, selenium, manganese, copper) that are used to form antioxidant enzymes (Friis and Michaelson, 1998). "Oxidative stress" occurs when there is an imbalance between the pro-oxidants and antioxidants, causing further damage to cells, proteins, and enzymes (Schwarz, 1996).

The synergy between nutrition, infection, and immune function has been well-documented. In Africa, research has been conducted on nutrition, immune function and several diseases, including measles (e.g., Dossetor et al, 1977; Axton, 1979; Waibale et al, 1999); tuberculosis (e.g., Kennedy et al, 1996; Madebo et al, 1997; Macallan, 1999a;

Niyongabo et al, 1999); and diarrhea (e.g., Vella et al, 1995; Sodeinde et al, 1997; Taniguchi et al, 1999).

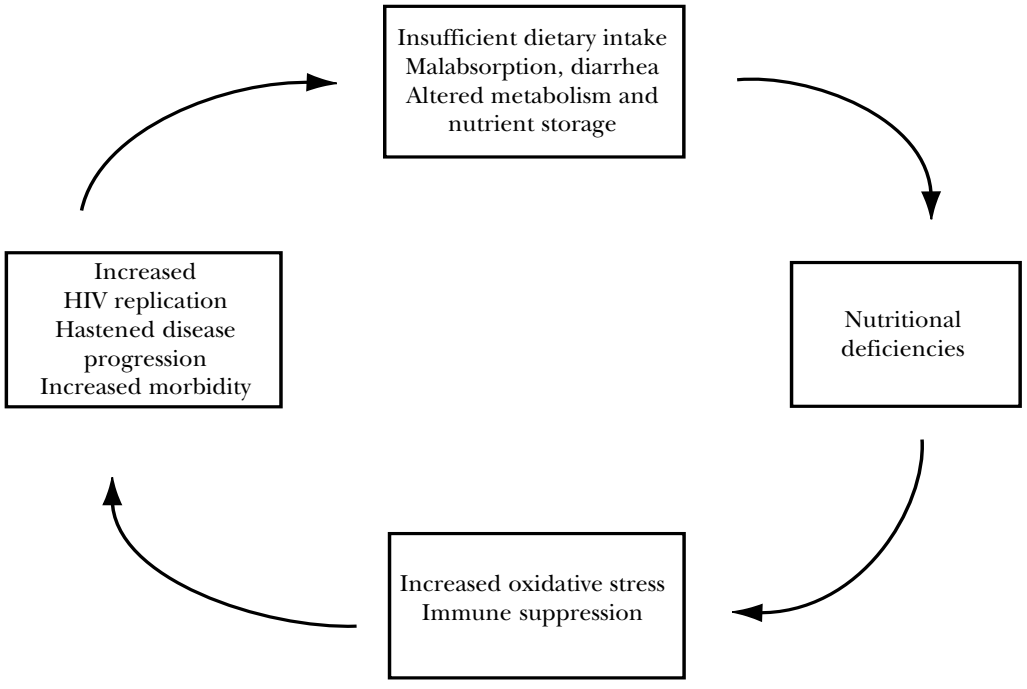
The relationship between HIV and nutrition, however, may be more complicated than the relationship between nutrition and other infectious diseases because the virus directly attacks and destroys the cells of the immune system. Nutritional deficiencies affect immune function in ways that may influence viral expression and replication, further affecting HIV disease progression and mortality (see **Figure 4**). Oxidative stress, for example, may indirectly hasten HIV replication (Semba and Tang, 1999). HIV infection also affects the production of hormones such as glucagon, insulin, epinephrine, and cortisol, which are involved in metabolism of carbohydrates, proteins, and fats. Elevated levels of these hormones contribute to weight loss and the wasting syndrome seen in most adult AIDS patients (Young, 1997). However, in infants and young children in developing countries, who are frequently malnourished and susceptible to many infectious diseases, HIV-related malnutrition may be difficult to differentiate from malnutrition from other causes in the absence of serologic tests to confirm HIV infection.

Malnutrition in PLWHA includes the following symptoms: weight loss; loss of muscle tissue and subcutaneous fat; vitamin and mineral deficiencies; reduced immune competence; and increased susceptibility to infection. Poor nutritional status may result from multiple causes: depressed appetite, poor nutrient intake, and limited food availability; chronic infection, malabsorption, metabolic disturbances, and muscle and tissue catabolism; fever, nausea, vomiting, and diarrhea; depression; and the side effects from drugs used to treat HIV-related infections. All of these causes are described in greater detail in this chapter.

B. The Social Context

Malnutrition associated with HIV infection has serious and direct implications for the quality of life of PLWHA. Weight loss is often the event that begins "a vicious cycle of increased fatigue and decreased physical activity, including the inability to prepare and consume food" (Babamento and Kotler, 1997). Malnutrition associated with HIV/

FIGURE 4. The Vicious Cycle of Micronutrient Deficiencies and Human Immunodeficiency Virus (HIV) Pathogenesis



Source: Semba and Tang (1999)

AIDS affects entire families when infected adults become too debilitated to work steadily, are unable to provide for themselves and their dependents, and require continuous care during bouts of illness.

Children, as well as adults, are profoundly affected by the indirect consequences of the AIDS epidemic in Africa. Even if they themselves are not infected, they are burdened by the illness and eventual death of one or both parents. For example, childhood malnutrition is one of the most severe and lasting consequences of parental death. A study in Kagera, Tanzania found that stunting among poor children under 5 (of unknown HIV status) was substantially higher for orphans (51 percent) than for children whose parents were both alive (39 percent) (The World Bank Group, 1997). Higher rates of stunting among orphans were believed to be due to the effects of vertically-transmitted HIV on the immune system; increased exposure to infectious diseases such as tuberculosis; disease-related poverty; and/or grief and psychological depression that interferes with caring practices, obtaining food, and providing meals.

In parts of Africa where farming is a primary occupation and nutritional requirements are usually met through local food production, HIV/AIDS in agricultural workers is affecting farm incomes, food productivity, and nutritional status. A study conducted by FAO in Malawi, Rwanda, and Tanzania predicted that by the year 2000, up to 25 percent of farm households could be affected by AIDS (Norse, 1991). In Zimbabwe, data suggest that there has been a 61 percent reduction in maize production, a 49 percent reduction in vegetable production, and a 37 percent reduction in groundnut production as a result of HIV/AIDS (Futures Group, 1999).

HIV/AIDS-related illness and mortality affects household food security through these mechanisms:

- the loss of adult on-farm or off-farm labor reduces household income;
- as a result, household savings, assets, and remittances are reduced;
- there is usually an increase in household expenditures for medical treatment, transportation, and other care-related needs; and
- at the same time the number of dependents relying on fewer productive household members for survival is increased (Topouzis and Hemrich, 1996).

The impact of HIV/AIDS on food security is expected to be especially severe in female-headed households and in areas where farm labor is already scarce (Hunter and Williamson, 1998; Barnett and Halswimmer, 1995).

C. Weight Loss and Wasting in HIV/AIDS

To understand the relationship between nutrition and HIV/AIDS, one must consider the effect of the disease on body size and composition (weight, lean body mass, body cell mass) as well as the effect on the functioning of the immune system. Nutrition plays a role in each of these conditions. One must also keep in mind that malnutrition may be a contributor to HIV disease progression as well as a consequence of the disease.

Body size and composition are used as indicators of protein-energy status, and these are most commonly expressed in terms of body weight and height (as described in Chapter II). Other important body composition indicators include body cell mass (the metabolically active, energy-exchanging tissue of the body), lean body or fat-free mass (an estimate of protein and mineral reserves, mainly stored in muscle), and skin-fold thickness (taken in different places of the body to estimate fat stores).

It is useful to bear in mind that in populations where malnutrition is endemic, body size and composition changes associated with protein-energy malnutrition are nearly always associated with deficiencies in vitamins and minerals, which are important for the functioning of the immune system. However, the reverse condition is not always true. A person who is suffering from mild or moderate micronutrient deficiency may not yet exhibit signs of abnormal weight, height, or body composition.

The wasting syndrome typically found in adult AIDS patients in Africa is a severe nutritional manifestation of the disease. Wasting is usually preceded by changes in appetite, repeated infections, weight fluctuations, and subtler changes in body composition, such as changes in lean body mass and body cell mass, which are more difficult

to measure than changes in weight alone (Babameto and Kotler, 1997).

Weight loss typically follows two patterns in PLWHA: slow and progressive weight loss from anorexia and gastrointestinal disturbances and rapid, episodic weight loss from secondary infections. Even relatively small losses in weight (5 percent) have been associated with decreased survival in people with AIDS and are therefore important to monitor (Macallan, 1999c).

Weight loss and wasting in PLWHA develop as a result of three overlapping processes:

- **Reductions in food intake**. This may be due to painful sores in the mouth, pharynx, and/or esophagus. Fatigue, depression, changes in mental state, and other psychosocial factors may also play a role by affecting appetite and interest in food. Economic factors affect food availability and the nutritional quality of the diet. Side effects from medications, including nausea, vomiting, metallic taste, diarrhea, abdominal cramps, and anorexia also result in lower dietary intakes that can cause weight loss associated with HIV/AIDS. Reductions in food intake are believed to be the most important cause of the slow and progressive weight loss experienced by PLWHA (Macallan, 1999c).

- **Nutrient malabsorption.** Malabsorption accompanies frequent bouts of diarrhea due to giardia, cryptosporidium, and other pathogens that affect persons with compromised immune systems. Some HIV-infected individuals have increased intestinal permeability and other intestinal defects even when asymptomatic (Keating et al, 1995). It is possible that HIV infection itself, particularly of the intestinal cells, may cause epithelial damage and nutrient malabsorption (Babameto and Kotler, 1997; Ullrich et al, 1989). Malabsorption of fats and carbohydrates is common at all stages of HIV infection in adults and children (Semba and Tang, 1999). Fat malabsorption, in turn affects the absorption and utilization of fat-soluble vitamins (e.g, vitamins A, E), further compromising nutrition and immune status.

- **Metabolic alterations. Table 2** summarizes the impact of infection on protein, fat, and energy (carbohydrate) metabolism. Infection results in increased energy and protein requirements[4], as well as in inefficient utilization and loss of nutrients (Macallan, 1999c).

  Changes in metabolism occur during HIV infection from severe reductions in food intake as well as from the immune system's response to the infection. When food is restricted, the body responds by altering insulin and glucagon production, which regulate the flow of sugar and other nutrients in the intestine, blood, liver, and other body tissues. Over time, the body uses up its carbohydrate stores from muscle and liver tissue and it begins to break down body protein to produce glucose. This process causes protein loss and muscle wasting.

  Wasting also results through a process known as cachexia, which is characterized by a significant loss of lean body mass resulting from metabolic changes that occur during the acute phase response to infection. During the acute phase response, the liver produces large amounts of specific proteins to bind and clear infectious agents. These proteins come, in large part, from the skeletal muscle. If the response, which is induced by immune-system cytokines, is prolonged, muscle wasting may become severe. Cachexia also affects appetite, sleep-wake cycles, and other body processes (Babameto and Kotler, 1997). As a result of these processes, HIV infection increases the body's protein and energy requirements to maintain weight and body composition.

Management of weight loss in HIV/AIDS is complicated by the fact that these three mechanisms are not mutually exclusive. Weight loss and wasting in people with AIDS may be the result of all three processes. For the first two causes of weight loss and wasting, malnutrition may be reduced by treating the immediate sources of the problem (e.g., oral thrush, mouth sores, other infections), providing preferred foods that are soft and well tolerated by the infected person, and increasing intake during periods of convalescence

[4] Existing studies suggest that infections result in a loss of 0.6 to 1.2 g of protein per kg body weight per day in adults when amino acids are mobilized from skeletal muscle (for gluconeogenesis, synthesis of immune proteins and enzymes) in response to the release of cytokines (e.g., interleukin-1, tumor necrosis factor). Losses are highest with diarrhea, dysentery, and other severe infections. For these reasons, protein requirements are substantially higher in HIV-infected individuals and persons suffering from chronic immune system stimulation. Furthermore, the energy requirement to replace lost protein is about 6-8 kcal/g of protein produced (Scrimshaw and SanGiovanni, 1997).

from acute infection (Cimoch, 1997). In contrast, weight loss and wasting due to metabolic changes cannot be reversed by feeding alone. Such programs tend to increase body fat but rarely improve body cell mass or increase the protein stores of wasted muscle (Cimoch, 1997; Macallan, 1999c).

Efforts to reverse muscle wasting in industrialized countries have relied on relatively expensive appetite stimulants and hormones such as testosterone and recombinant growth hormone (costing $1000/week). A randomized trial in the USA, however, provided a less expensive supplement containing the amino-acid glutamine (40g/day) together with antioxidants (vitamins C and E, beta-carotene, selenium, and N-acetyl cysteine) at recommended daily allowance (RDA) levels to 12 HIV-infected men and women, who had already experienced significant weight loss, for 12 weeks (Shabert et al, 1999). Nine similar subjects received a placebo supplement. All participants received nutritional counseling. The participants receiving the nutritional supplement gained and maintained significantly more body weight than the control subjects over the 3-month period (2.2 kg), including 1.8 kg in body cell mass (BCM). This compared with a change in BCM of only 0.4 kg in the control subjects ($p<0.007$). The improvement in BCM was present after controlling for dietary

TABLE 2. Metabolic Alterations that Accompany Acute Infections

Protein
Increased urinary nitrogen loss Increased protein turnover Decreased skeletal muscle protein synthesis Increased skeletal muscle breakdown Increased hepatic protein synthesis
Lipid (fat)
Hypertriglyceridemia Increased hepatic de novo fatty acid synthesis Increased hepatic triglyceride esterification Increased very low-density lipoprotein production Decreased peripheral lipoprotein lipase activity Increased adipocyte triglyceride lipase
Carbohydrate
Hyperglycemia Insulin resistance Increased peripheral glucose utilization Increased gluconeogenesis

Source: Babameto and Kotler (1997).

RESEARCH PROFILE: COTE D'IVOIRE

Nutritional Status, Dietary Intake, and HIV

Researchers recognized that while data on prevalence of malnutrition and dietary intake in HIV-infected persons is widely available in industrialized countries, it is often absent in African settings where endemic malnutrition and lack of nutrition management are common. A cross-sectional study was undertaken in Abidjan, Cote d'Ivoire, to evaluate nutritional status and dietary intakes of 100 adult HIV-infected outpatients at different stages of infection. Outcome measures included weight, height, triceps skinfold, arm circumference, body mass index, muscular circumference, and weight loss. The 24-hour recall method was used to evaluate dietary intake. Two-thirds of the patients were malnourished according to body mass index values. Anthropometric values were lower in symptomatic patients (classified by WHO system) and in patients with CD4 cell counts < 200. Weight loss was greater in symptomatic patients but was unrelated to CD4 cell count. Appetite problems were present in 45 percent of the patients, and particularly in symptomatic patients. Dietary intakes were below recommended levels for healthy adults for protein and energy. Patients with chronic diarrhea had lower intakes of protein, carbohydrates, and fats. Clinical events associated with malnutrition and weight loss included chronic diarrhea, chronic fever, appetite loss, and pulmonary tuberculosis. The researchers concluded that secondary infections adversely affect dietary intake and the nutritional status of PLWHA.

Source: Castetbon K, Kadio A, Bondurand A et al (1997).

intake. Glutamine (GLN) is produced in skeletal muscle and used by the immune system, the gastrointestinal tract, and other organs. Muscle wasting occurs, in part, to satisfy the body's need for GLN during infection. This was one of the first studies to show that nutritional supplementation, including the amino acid GLN, can restore body cell mass in HIV-infected persons already experiencing weight loss and muscle-wasting (Shabert et al, 1999).

Other types of dietary supplements may also benefit AIDS patients who have experienced weight loss. Some fatty acids, such as omega-3 fatty acids common in fish oils and some seeds, are required for the body to respond to inflammation and to reduce the impact of cytokines that promote wasting (e.g., interleukin-1 and tumor necrosis factor). Researchers in the USA gave a daily dietary fish oil supplement (18g/day) to 16 men with AIDS for 10 weeks and monitored weight gain. An unsupplemented control group was also followed. Fish oil supplementation resulted in weight gain, but only among patients who did not develop new AIDS complications. The researchers concluded that fish oil supplementation may benefit some people with AIDS but may not overcome the metabolic consequences of acute infections in others (Hellerstein et al, 1996).

In another study, researchers in the USA found that weight gain and/or weight maintenance could be achieved among asymptomatic HIV-infected individuals, and among HIV-positive people in the early stages of AIDS with no secondary infections, who received at least one daily, high-energy, high-protein, liquid food supplement along with nutritional counseling recommending a high-protein diet and foods that minimize gastrointestinal complications. In participants who had already developed secondary infections, however, weight loss continued to occur despite supplements and nutritional counseling (Stack et al, 1996).

The extent to which nutritional therapy can reverse weight loss and wasting in PLWHA in Africa is largely unknown. From the preceding studies it appears that the impact of nutritional interventions will depend, in part, upon the stage of disease as well as the types of nutritional management provided. This has important implications for PLWHA in Africa. In the early stages of HIV infection — especially before the onset of secondary infections — simple, affordable nutrition supplementation and counseling may be feasible and have a positive impact on body composition and weight. But, unfortunately, relatively few HIV-infected people in Africa learn of their status at these early stages of infection because HIV counseling and testing services are not available or are underutilized. In the later stages of disease, when most PLWHA learn of their status, nutritional supplementation and counseling appear less likely to be effective.

Finally, it is important to mention that whereas weight loss and wasting are common risk factors for defining AIDS and predicting shortened survival in adults, these conditions are less useful predictors of AIDS among African children who frequently suffer from malnutrition and infection-related growth faltering in the absence of HIV infection. Growth failure has been recognized as a major feature of pediatric HIV in Africa since the early 1990s, as described in studies from Burkina Faso (Prazuck et al, 1993); Cote d'Ivoire (Mutombo et al, 1995); Tanzania (Mbone et al, 1991); Uganda (Berhane et al, 1997); Zimbabwe (Ticklay et al, 1997); and Rwanda (Lepage et al, 1996; Spira et al, 1999). However, because children are smaller than adults, a loss in weight of 10 percent, which is consistent with the definition of AIDS wasting syndrome in adults, can amount to as little as 1 kg. Therefore, it is important to regularly monitor the growth of all infants and young children to document growth trends and to identify the onset of growth faltering and/or weight loss as early as possible. Weight loss alone should not be used to diagnose HIV infection in children or adults.

D. Vitamins and Minerals in HIV/AIDS

Many vitamins and minerals (also referred to as micronutrients) are important to the HIV/nutrition relationship due to their critical roles in cellular differentiation, enzymatic processes, immune system reactions, and other body functions described previously (Fawzi and Hunter, 1998). **Table 3** summarizes the roles of different vitamins and minerals in supporting body functions functions and lists some of the foods that contain them.

The role of micronutrients in other infectious diseases, such as measles, diarrhea, and respiratory infections has been extensively studied and it is known that several vitamins and minerals are

required by the immune system and major organs to fight infectious pathogens. Persons with inadequate intakes, blood levels, or body stores of these micronutrients have difficulty resisting infection. As a result, the role of micronutrients in HIV/AIDS takes on special importance in individuals and populations with marginal or low micronutrient intakes (Friis and Michaelson, 1998). This applies to most of AIDS-affected Africa, where, as described earlier, micronutrient deficiency is endemic.

Studies from both industrialized and developing countries have confirmed that HIV-infected individuals have decreased absorption, excessive urinary losses, and low blood concentrations of vitamins A, B_1, B_2, B_6, B_{12}, C, E, as well as of folate, beta-carotene, selenium, zinc, and magnesium (Friis and Michaelsen, 1998; Tang and Smit, 1998). At present, it is not known whether these deficiencies are independent markers of disease progression resulting from a compromised immune system, or whether they are causally related to the development or exacerbation of symptoms of HIV/AIDS. This distinction is important in order to determine whether the nutritional deficiencies can be reversed, and whether nutritional therapy and management can slow or alter the course of the disease. Studies of the role of different micronutrients in HIV transmission, disease progression, and mortality are summarized in subsections 1 and 2. Issues to consider when interpreting these findings or extrapolating them to African populations are also discussed.

1. Micronutrients and HIV disease progression and mortality

Several reviews have been published recently on the role of micronutrients in HIV disease progression and mortality (Baum and Shor-Posner, 1998; Fawzi and Hunter, 1998; Friis and Michaelson, 1998; Tang and Smit, 1998; Semba and Tang, 1999). These reviews have concluded that micronutrient deficiencies associated with HIV vary across populations and according to disease stage; are associated with an accelerated progression of HIV infection to AIDS; and are predictive of AIDS-related mortality.

These observational associations were initially promising because micronutrient supplementation, unlike many other AIDS treatments, has the potential in Africa to be an affordable and relatively easy to deliver public health measure. The findings from micronutrient supplementation trials, however, have been mixed. The roles of specific micronutrients in HIV disease progression and mortality, and the findings from published intervention trials are summarized below.

RESEARCH PROFILE: ZAMBIA

Micronutrient Supplementation and Diarrhea-wasting Syndrome

The home-care service of Ndola Central Hospital was the site of a study to explore the problem of diarrhea-related wasting in HIV-infected patients, and to determine whether the clinical response to the diarrhea treatment drug, albendazole, might be improved by oral micronutrient therapy. HIV+ patients with persistent diarrhea (for more than one month) were randomly allocated to receive 800 mg of albendazole twice daily for 14 days plus a placebo (n=69) or the same regimen of albendazole plus a daily micronutrient supplement containing vitamins A, C, E, selenium, and zinc (n=66). Patients were followed for up to 3 months and the proportion of patient-weeks during which diarrhea was experienced was compared. Patient-weeks with diarrhea declined over time but were not different in the two treatment groups. Deficiencies at enrollment of vitamins A and E, affecting more than half of study participants, predicted mortality within the first month irrespective of treatment group. The researchers believe that micronutrient supplementation was not effective because of impaired absorption. They concluded that, although micronutrient deficiency is predictive of early death in Zambian HIV-patients with persistent diarrhea, short-term, oral micronutrient supplementation does not overcome the deficiency, or influence morbidity and mortality.

Source: Kelly P, Musonda R, Kafwembe E et al (1999).

TABLE 3. The Role of Some Vitamins and Minerals in the Body and Sources of Nutrients

Nutrient	Its Role	Sources
Vitamin A	Required for maintenance of epithelial cells, mucous membranes, and skin. Needed for immune system function and resistance to infections. Ensures good vision. Needed for bone growth.	Full-cream milk (when fortified), cheese, butter, red palm oil, fish oil, eggs, liver, carrots, mangos, papaya, pumpkin, green leafy vegetables, yellow sweet potatoes.
Vitamin B_1/Thiamine	Used in energy metabolism, supports appetite, and central nervous system functions.	Whole-grain cereals, meat, poultry, fish, liver, milk, eggs, oil, seeds, and legumes.
Vitamin B_2/Riboflavin	Used in energy metabolism, supports normal vision, health and integrity of skin.	Milk, eggs, liver, meat, fish, yogurt, green leaves, whole-grained cereals, and legumes.
Vitamin B_3/Niacin	Essential for energy metabolism, supports health and integrity of skin, nervous and digestive systems.	Milk, eggs, meat, poultry, fish, peanuts, whole-grained cereals, unpolished rice.
Vitamin B_6	Facilitates metabolism and absorption of fats and proteins, converts tryptophan to niacin, helps to make red blood cells. Some TB drugs cause B_6 deficiency.	Legumes (white beans), potatoes, meats, fish, poultry, shellfish, watermelon, oil seeds, maize, avocado, broccoli, green leafy vegetables. Alcohol destroys vitamin B_6.
Folate (folic acid)	Required for synthesis of new cells, especially red blood cells and gastrointestinal cells.	Liver, green leafy vegetables, fish, legumes, groundnuts, oil seeds.
Vitamin B_{12}	Required for synthesis of new cells, helps to maintain nerve cells. Works together with folate.	Meat, fish, poultry, shellfish, cheese, eggs, milk.
Vitamin C	Helps the body to use calcium and other nutrients to build bones and blood vessel walls. Increases non-heme iron absorption. Increases resistance to infection and acts as an antioxidant. Important for protein metabolism.	Citrus fruits such as baobob, guava, oranges and lemons; cabbage, green leaves, tomatoes, peppers, potatoes, yams, cooking plantains, and fresh milk. Vitamin C is lost when food is cut up, heated, or left standing after cooking.
Vitamin D	Required for mineralization of bones and teeth.	Produced by skin on exposure to sunshine; milk, butter, cheese, fatty fish, eggs, liver.
Vitamin E	Acts as an antioxidant. Protects cell membranes and metabolism, especially red and white blood cells. Protects vitamin A and other fats from oxidation. Facilitates resistance against diseases, particularly in lungs.	Green and leafy vegetables, vegetable oils, wheat germ, whole-grain products, butter, liver, egg yolk, peanuts, milk fat, nuts, seeds.
Iron	Required to make hemoglobin for red bloods cells, and to transport oxygen from lungs to cells throughout the body. Acts as an anti-oxidant. Required for utilization of energy and metabolism by cells.	Heme iron sources (high absorption) include red meat, liver, fish, poultry, shellfish. Non-heme iron sources (low absorption) include eggs, legumes, peanuts, some cereals and dried fruits. Vitamin C, heme iron foods, and some fermented foods increase non-heme iron absorption. Tea, coffee, and some grains and green leafy vegetables (with phytate) decrease non-heme iron absorption.

TABLE 3. cont.

Nutrient	Its Role	Sources
Calcium	Required for building strong bones and teeth. Important for normal heart and muscle functions, blood clotting and pressure, and immune defenses.	Milk, yoghurt, cheese, green leafy vegetables, broccoli, dried fish with bones that are eaten, legumes, peas.
Zinc	Important for function of many enzymes. Acts as an anti-oxidant. Involved with making genetic material and proteins, immune reactions, transport of vitamin A, taste perception, wound healing, and sperm production.	Meats, fish, poultry, shellfish, whole grain cereals, legumes, peanuts, milk, cheese, yoghurt, vegetables.
Selenium	Acts as an antioxidant together with vitamin E. Prevents the impairing of heart muscles.	Meat, eggs, seafood, whole grains, plants grown in selenium rich soil.
Magnesium	Important for building strong bones and teeth, protein synthesis, muscle contraction, transmission of nerve impulses.	Nuts, legumes, whole grain cereals, dark green vegetables, seafood.
Iodine	Ensures the development and the proper functioning of the brain and of the nervous system. Important for growth, development, metabolism.	Seafood, iodized salt, plants grown in iodine-rich soil.

Sources: Ndiaye (1997); Savage King and Burgess (1995); Whitney et al (1990).

- **Vitamin A.** Of all the micronutrients, the role of vitamin A in HIV infection has received the greatest attention in Africa. This is because of its well-known role in affecting child morbidity and mortality, as well as early observations that vitamin A status was associated with increased risks of MTCT of HIV (Semba et al, 1994b); HIV viral load in breastmilk and vaginal secretions (Nduati et al, 1995; John et al, 1997); progression to AIDS (Tang et al, 1993); adult survival (Semba et al, 1994a); and infant morbidity (Coutsoudis et al, 1995) and mortality (Dushimimana et al, 1992). The potential for vitamin A supplementation to positively impact the course of HIV/AIDS was promising to pursue since vitamin A is beneficial in HIV-negative populations, is inexpensive, and relatively easy to administer with minimal side effects.

  Vitamin A deficiency may be caused by insufficient dietary intake of vitamin A-rich food (**Table 3**); malabsorption; impaired storage (because of liver disease); and/or increased utilization or urinary loss of vitamin A during acute and chronic infection (Semba, 1997). Vitamin A deficiency causes anemia, growth retardation, and xeropthalmia (corneal drying that if untreated results in scarring and blindness); it increases the incidence and/or severity of many infections (including diarrhea, pneumonia, measles, other respiratory infections); and it increases the risk of child (Sommer and West, 1996) and maternal mortality (West et al, 1999). While vitamin A deficiency is relatively rare among HIV-negative adults in industrialized countries, up to one-third of HIV-positive adults in industrialized countries may be vitamin A deficient. One study estimated that up to 60 percent of HIV-infected pregnant women in developing countries suffer from vitamin A deficiency (Nimmagadda et al, 1998).

  Several studies in Africa have measured the impact of vitamin A supplementation on various HIV-related outcomes in children. In South Africa, vitamin A supplementation of HIV-infected children reduced diarrhea morbidity by about 50 percent in one study (Coutsoudis et al, 1995), and improved immune status in another study (Hussey et al, 1996). In Tanzania, vitamin A supplementation reduced all-cause mortality by 63 percent among HIV-infected children aged 6 months to 5 years, and was associated with a 68 percent

reduction in AIDS-related deaths and a 92 percent reduction in diarrhea-related deaths (Fawzi et al, 1999).

In adult studies conducted in the USA and Africa, vitamin A and/or beta-carotene supplementation had no significant or prolonged impact on HIV viral load (Semba et al, 1998), immune status (Coodley et al, 1996; Fawzi et al, 1998), diarrhea morbidity (Kelly et al, 1999), or prenatal and postnatal morbidity in women (Kennedy et al, 2000). One observational study found that very high intakes of vitamin A (> 20,000 IU/day) were actually associated with increased mortality (Tang et al, 1996). The impact of vitamin A supplementation on MTCT and other birth outcomes is described in the following subsection.

- **Vitamin B_{12}.** Vitamin B_{12} deficiency is relatively uncommon in healthy, non-vegetarian populations. However, many studies of people with HIV in the USA report low serum B_{12} levels even among asymptomatic persons. Low serum B_{12} levels are associated with neurological abnormalities (e.g., peripheral neuropathy, myelopathy); impaired cognition (e.g., information processing, problem-solving); reduced CD4 T-cell counts; increased bone marrow toxicity associated with use of ziduvodine, an antiretroviral (ARV) drug; and increased mortality (Tang and Smit, 1998). A 9-year study among homosexual and bisexual men with HIV/AIDS in the USA found that men with low serum B_{12} at enrollment (< 120 pmol/L) had significantly shorter AIDS-free survival times than men with adequate B_{12}, after taking into account HIV-related symptoms, CD4 cell count, age, ARV use, and other potentially confounding variables (Tang et al, 1997a). Another study of USA men found that improvements in B_{12} levels were associated with increases in CD4 cell count. Normalization of vitamin A and zinc levels had a similar but smaller effect (Baum et al, 1995). No studies of vitamin B_{12} and HIV/AIDS in Africa were identified.

- **Folate.** Folate (also known as folic acid) works closely with vitamin B_{12}, but its role in HIV/AIDS remains unclear. Folic acid is required for the enzymes that produce DNA for replicating and growing cells, including those of the gastrointestinal (GI) tract, blood, and growing fetus. Deficiency results in impaired cell division and protein synthesis, causing megaloblastic anemia. Folic acid is recycled in the body. If the GI tract is damaged, as is common in HIV-related diarrhea or with chronic alcohol use, folic acid reabsorption may be impaired, setting off a cycle where deficiency results in further GI tract deterioration and malabsorption of other nutrients.

  Studies to date have not shown a relationship between folate deficiency and HIV-related outcomes. Low serum folate (measured once at enrollment) was not associated with HIV/AIDS disease progression and CD4 cell decline in the same study cited above that indicated an important role for B_{12} deficiency (Tang et al, 1997a). However, only 8 percent of men were initially folate deficient (< 3.4 nmol/L) and more than 50 percent of the men took B-complex vitamin supplements during the study. A study in Malawi found that red blood cell folate levels were not significantly different among asymptomatic, HIV-infected, anemic, pregnant women and anemic women who were not HIV-infected in Malawi (Van den Broek et al, 1998).

  It may be important to note that folate is vulnerable to interaction with various drugs. For example, aspirin and oral contraceptives interfere with folate absorption and metabolism (Thomas, 1995). On the other hand, the efficacy of sulfadoxine-pyrimethamine (SP), an antimalarial drug used to treat falciparum malaria, may be reduced by folate supplementation (van Hensbroek et al, 1995). Therefore, although existing studies do not indicate a relationship between folate and HIV, the potential interaction between folate and drugs taken by HIV-infected persons should be taken into consideration when evaluating the nutritional needs of PLWHA.

- **Vitamin E.** Vitamin E is necessary for the proper functioning of the immune system and it increases humoral and cell-mediated immune responses, including antibody production, phagocytic and lymphocytic responses, and resistance to viral and infectious diseases (Odeleye and Watson, 1991). Vitamin E is one of the few nutrients (another is

vitamin A) for which supplementation at higher than daily recommended levels has been shown to increase immune response and resistance to disease (Meydani and Hayek, 1992). The oxidative stress created by HIV and related opportunistic infections increases the utilization of the antioxidant vitamin E, possibly leading to deficiency. Vitamin E deficiency, in turn, further debilitates the immune system because of its role in immune stimulation and functioning, leaving PLWHA more susceptible to opportunistic infections.

Studies in the USA found that high baseline serum vitamin E levels were associated with decreased HIV progression after taking into account HIV-related symptoms, CD4 cell count, age, ARV use, and other potentially confounding variables (Tang et al, 1997b). Men with serum vitamin E levels greater than or equal to 23.5 mmol/l had 34 percent longer until first AIDS diagnosis compared with men with low serum vitamin E levels (Tang et al, 1997b). Another study in Canada found that 3 months of supplementation with vitamin E (800 IU) and vitamin C (1000 mg) significantly reduced oxidative stress and HIV viral load (Allard et al, 1998). A study in Zambia, among AIDS patients suffering from persistent diarrhea, found that vitamin E deficiency at enrollment predicted mortality in the following month (see Box, "Research Profile: Zambia—Micronutrient Supplementation and Diarrhea-wasting Syndrome"). However, oral supplementation with vitamin E and other nutrients did not affect either mortality or diarrhea morbidity, possibly because of severe fat malabsorption accompanying the late-stage disease (Kelly et al, 1999).

- **Selenium.** Selenium deficiency is unusual in healthy populations and rarely measured outside of specialized clinical studies. Selenium deficiency impairs the immune system and has been associated with faster HIV disease progression and reduced survival in adults (Baum and Shor Posner, 1998) and children (Campa et al, 1999). Selenium is believed to play an important role in metabolizing reactive oxygen species ("free radicals") and reducing oxidative stress because it is an essential cofactor for glutathione perodixase, an antioxidant enzyme. In animal models, selenium deficiency has been shown to increase viral pathogenicity (Beck 2000). Selenium deficiency, therefore, may contribute to HIV replication and possibly also to increasing the infectiousness of the virus (Friis and Michaelsen, 1998).

  One study in the USA found that selenium deficiency (measured over time) was significantly associated with HIV-related death, after taking into account CD4 cell counts at baseline and over time, use of ARV drugs, and other nutritional deficiencies (protein, zinc, and vitamins A, B_6, B_{12}, and E). In fact, it was the only nutritional deficiency that was independently predictive of survival after controlling for these other nutrients (Baum et al, 1997).

  Only one study of the effects of selenium supplementation was identified. This study provided oral selenium (100 micrograms/d), beta-carotene (60 mg/d), or a placebo for one year to 45 selenium and vitamin A deficient HIV-infected study subjects in France. Selenium supplements increased antioxidant enzyme functions significantly and the effects were greater than those observed with beta-carotene supplementation (Delmas-Beauvieux et al, 1996). These findings suggest that selenium (and beta-carotene) supplementation may reduce the impact of oxidative stress on HIV disease. No studies on selenium and HIV/AIDS in Africa were identified.

- **Zinc.** Zinc is an essential component of the immune system and it is important for the development of non-specific and cell-mediated immunity (particularly CD4 cells). Zinc is also required for the gene expression and the normal development of many tissues and cells. Zinc is an important component of many proteins, hormones, and enzymes. Mild and marginal zinc deficiency, believed to be very common in Africa, results in depressed immunity; impaired taste and smell; damage to the epithelial lining of the intestine and respiratory tract; and impaired memory, among other effects (Shankar and Prasad, 1998). Severe zinc deficiency results in severe immune depression, frequent diarrhea and other infections, as well as mental disturbances.

  Zinc plays a role in HIV because the virus requires zinc for gene expression, replication,

and integration (Baum et al, 2000). Thus, persons with HIV may have low plasma zinc levels yet higher zinc intakes may be associated with faster HIV replication and disease progression (as observed below). High intakes of zinc (in the absence of HIV) may interfere with copper and iron utilization, and very high intakes (more than 20 times the RDA) have produced significant immune system impairments in healthy adults (Chandra, 1997). Zinc also inhibits tumor necrosis factor (TNF), a cytokine that is important in triggering the process of wasting in HIV described in Chapter III, section C. Zinc deficiency, on the other hand, affects T-cell activity, including the secretion of numerous cytokines that affect HIV disease progression (Baum et al, 2000; Mocchegiani and Muzzioli, 2000; Rosenberg and Fauci, 1990).

There have been relatively few studies of zinc and HIV/AIDS and no studies in Africa were identified. In the USA, low serum zinc levels were associated with HIV disease progression and mortality in adult intravenous drug users (Baum et al, 1997). On the other hand, Tang et al (1996) found that high intakes of zinc (from diets and supplements) were associated with reduced survival in HIV-infected men. Men consuming 14-20 mg/d had a relative mortality risk of 1.73 during follow-up, and those with intakes greater than 20 mg/d had a relative mortality risk of 1.91, after adjusting for CD4 cell count, age, use of ARV, total energy intake, and presence of disease symptoms (Tang et al, 1996). The recommended daily allowance for zinc in healthy adult American men is 15 mg/d.

Zinc supplementation among AIDS patients, however, has shown substantial benefits. In a study in Italy, daily zinc supplementation (200 mg/d) for one month reduced the incidence of opportunistic infections (particularly *pneumocystis carinii* and *candida*), stabilized weight, and improved CD4 cell counts among adults with AIDS who were also receiving ARV therapy as compared with controls who received ARVs but no zinc supplement (Mocchegiani et al, 1995; Mocchegiani and Muzzioli, 2000).

These findings suggest zinc supplementation should be approached cautiously and must take into account dietary intake of the mineral. Zinc supplementation, in short courses and carefully monitored, may be useful for strengthening resistance to opportunistic infections among persons with AIDS (Mocchegiani and Muzzioli, 2000).

- **Iron and anemias.** Iron is vital for all cells to generate energy. Iron is found in muscle, in blood (hemoglobin), and in many enzymes required for metabolism. Iron is required to produce new cells, amino acids, and hormones, and it is transported throughout the body to be used as needed. Iron is stored in the liver and used in large quantities by the bone marrow to make new red blood cells. Iron is recycled by the body for its many uses. When stores are depleted and dietary intake cannot compensate for these requirements, then iron deficiency occurs. Iron deficiency is measured through several indicators but the most commonly reported indicator is hemoglobin.

  Anemia is a condition where there are too few red blood cells (due to slowed production or accelerated destruction), or the red blood cells are immature, small, and carry too little hemoglobin (oxygen) to the tissues. Anemia is defined as hemoglobin levels less than 13 g/dl for men; 12 g/dl for non-pregnant women; and less than 11g/dl for pregnant women and children. There are multiple causes of anemia in Africa, including iron deficiency, malaria, hookworm infection, and other persistent infections.

  Anemia is a common problem among PLWHA, affecting asymptomatic HIV-infected adults and children, as well as people with AIDS (Castaldo et al, 1996; Adewuyi and Chitsike, 1994; Fleming, 1989). The causes of anemia associated with HIV/AIDS are not well understood. Anemia may result from cytokine-induced suppression of red blood cell production; chronic inflammation; opportunistic infections; and/or reductions in dietary intake (including iron), absorption, and retention. Anemia may also be caused by certain antiretroviral drugs (e.g., ZDV, which supresses bone marrow function and synthesis of red blood cells), as well as by nutritional deficiencies of iron, folate, riboflavin, vitamin A, and vitamin B_{12}.

Studies have found that anemia is associated with HIV disease progression and a two to four-fold increased risk of death in HIV-infected individuals. The risk increases with the severity of the anemia (Moore et al, 1998). One longitudinal study in Europe found that risk of death increased by 57 percent for each 1g/dl drop in hemoglobin in HIV-infected subjects, after controlling for CD4 cell counts, viral load, and use of ARV drugs (Mocroft et al, 1999). This risk was greater than the risks observed with a 50 percent reduction in CD4 cell count and a "log" increase in HIV viral load. On the other hand, studies also suggest that reversing anemia can slow HIV disease progression and prolong survival (Sullivan et al, 1998; Moore et al, 1998; Moore, 1999).

Anemia affects more than half of all pregnant women in Africa. The condition appears to be more common among HIV-infected pregnant women than the general antenatal population according to studies in Malawi (see Box, "Research Profile: Malawi—Anemia, Pregnancy and HIV") and Burkina Faso. The Malawi study, carried out among 155 anemic pregnant women attending antenatal clinics, found that asymptomatic HIV-infected women were twice as likely to be anemic as uninfected women, after taking into consideration folate, B_{12}, and serum retinol levels, and coexisting inflammation (Van den Broek et al, 1998). In Burkina Faso, HIV-infected pregnant women were more likely to be anemic (78 percent) than uninfected pregnant women (64 percent; $p < 0.001$) (Meda et al, 1999). In both studies, researchers did not measure malaria parasitemia, which is a common cause of anemia at least among first time mothers in Africa (Verhoeff et al, 1999).

These studies suggest that interventions to reduce or reverse anemia among PLWHA may prolong survival. However, anemia may be especially common among HIV-infected pregnant women, with implications for programs using ARVs to reduce mother-to-child tranmission of HIV.

It is worthwhile to mention that although anemia is common among PLWHA, advanced HIV disease may also be characterized by increases in iron stores in bone marrow, muscle, liver, and other cells (de Monye et al, 1999). This accumulation of iron is likely to be due to the body's attempts to withhold iron from the plasma, although other factors (e.g., ZDV use, cigarette smoking, and blood transfusions) may play a role (Boelaert et al, 1996). Increased iron stores can predispose to microbial infection and also cause oxidative stress, with implications for HIV disease progression. Additional research is required to identify approaches for managing this

RESEARCH PROFILE: MALAWI

Anemia, Pregnancy, and HIV

Researchers in Blantyre, Malawi were interested in learning whether asymptomatic HIV infection was associated with increased risk of anemia during pregnancy. They recruited 155 women with hemoglobin levels (Hb) below 10.5 g/dl who were attending antenatal clinics at the Queen Elizabeth Central Hospital. The background HIV-seroprevalence rate among women attending the antenatal clinic is 30.2 percent. Among the anemic women recruited, 47.1 percent were HIV-positive, which was significantly higher than the prevalence in the general antenatal population ($p < 0.001$). HIV-infected women were significantly more likely to be suffering from chronic inflammation (as measured by C-reactive protein levels), but reduced Hb was also observed in HIV-infected women without inflammation. Serum retinol, B_{12} and folate levels were not significantly different among the HIV-infected and uninfected women. The researchers conclude that HIV affects the production of red blood cells, and this impact is independent of nutritional status or opportunistic infection. They also note that HIV-infection should be suspected among anemic women living in areas of high HIV prevalence who do not respond to iron-folate supplementation.

Source: Van den Broek NR, White SA and Neilson JP (1998).

condition in PLWHA, including research in Africa, where iron deficiency is also common.

- **Other vitamins and minerals**. Virtually all other vitamins and minerals affect the immune system or are affected by infection (see **Table 3**). Observational studies have found that deficiencies in vitamins B_1 (thiamine), B_2 (riboflavin), B_3 (niacin), B_6 (pyridoxine), and C are more common among HIV-infected men living in industrialized countries than among the uninfected in the same populations. High or increased intakes of these vitamins were associated, for the most part, with slower progression to AIDS in US male homosexuals (Tang et al, 1996; Abrams et al, 1993) and in black South African AIDS patients (Kanter et al, 1999).

The observations that many nutrient deficiencies occur together and that diets in Africa are likely to be deficient in several nutrients point to the need to examine the impact of multiple micronutrient supplements on HIV-related outcomes. One study in South Africa found that multiple supplements slowed progression to AIDS and death when given with other drug therapies (Kanter et al, 1998). A study in Tanzania of the impact of multivitamin supplementation during pregnancy on HIV-related birth outcomes is described in the following subsection (see Box, "Research Profile: Tanzania—Multivitamin Supplementation, MTCT and other Pregnancy Outcomes").

2. Micronutrients and mother-to-child transmission of HIV

The relationship between HIV/AIDS and nutrition is important for pregnant women, as well as for infants who are being infected in large numbers through the mechanism of mother-to-child transmission (MTCT) of HIV (also referred to as vertical or perinatal transmission). MTCT can occur during pregnancy (when HIV crosses the placenta); during labor or delivery (when the infant comes in contact with the mother's HIV-infected body fluids); or during the postpartum period through breastfeeding.

Among HIV-infected women, high viral load (due to recent or advanced infection) and low CD4 cell counts increase the likelihood that a mother will pass on HIV to her baby during pregnancy, at the time of delivery, or during breastfeeding. As discussed in the previous sections, malnutrition-facilitated immune suppression may contribute to increased viral replication and concentration in the blood. If this is the case, malnutrition during pregnancy may increase the risk of MTCT of HIV (Semba, 1997). In addition, some micronutrient deficiencies during pregnancy (e.g., vitamin A,

RESEARCH PROFILE: TANZANIA

Multivitamin Supplementation, MTCT, and Other Pregnancy Outcomes

Researchers in Tanzania assessed the impact of vitamin A and multivitamin supplementation on T-cell counts and on various pregnancy outcomes among HIV-infected women. During the study, 1075 HIV-infected pregnant women received daily either placebo (n=267); vitamin A (5000 IU preformed vitamin A with 30 mg beta-carotene; n=269); a multivitamin (n=270) that contained vitamin A, vitamins B_1 (20 mg), B_2 (20 mg), B_6 (25 mg), niacin (100 mg), B_{12} (50 micrograms), C (500 mg), E (30 mg), and folic acid (0.8 mg); or the same multivitamin excluding vitamin A (n=269). All women also received iron and folate tablets daily and weekly prophylactic chloroquine. Multivitamin supplementation reduced the risk of fetal death by 39 percent; the risk of low birth weight by 44 percent; the risk of severe pre-term birth (before 34 weeks) by 39 percent; and the risk of small size for gestational age at birth by 43 percent. The beneficial impact of multivitamins on birth weight was observed only among babies who were HIV-negative at birth. Multivitamin supplementation also increased T-cell counts of the mothers significantly. Vitamin A alone, on the other hand, did not affect any of these outcomes. Neither supplement reduced MTCT during pregnancy, delivery, or the early breastfeeding period. The impact of multivitamin supplementation during lactation on breastfeeding-related HIV transmission is being studied.

Sources: Fawzi WW, Msamanga SI, Spiegelman D et al (1998); Fawzi WW, Msamanga G, Hunter D et al (2000).

zinc) result in low fetal nutrient stores, which in turn affect an infant's immune system, possibly also increasing vulnerability to HIV (Friis and Michaelsen, 1998).

Pregnancy is a particularly vulnerable time for African women because their nutritional requirements for energy, vitamins, and minerals increase by up to 30 percent, yet their usual daily intakes are frequently below recommended levels and allowances for healthy pregnant women. Malnutrition during pregnancy, therefore, may further erode HIV-infected women's immune status and make them more vulnerable to disease progression, although this hypothesis has not yet been proven.

The same hypothesis may also hold for HIV-infected women during breastfeeding. For example, the energy cost of exclusive breastfeeding is greater than 500 calories per day and breastfeeding increases maternal requirements for many nutrients, particularly iron, zinc, copper, folic acid, calcium, and vitamin D (Baker et al, 1996). A recent study in Kenya observed that breastfeeding HIV-infected mothers lost more weight and were more likely to die in the 2 years following delivery than HIV-infected mothers who did not breastfeed (Nduati et al, 2000a).

If HIV-related indicators can be improved by bettering maternal nutritional status, then prenatal and postnatal micronutrient and energy supplementation could prove to be an important intervention (Phuapradit, 1998; Friis and Michaelsen, 1998). Supplementation interventions can benefit all pregnant and postnatal women, not only those who are HIV-infected, and such programs can be introduced independently from other HIV services. However, as indicated in the previous subsection, relatively few intervention studies have been carried out in African populations to assess the impact of nutritional supplementation on HIV-related outcomes. This section will summarize available research on micronutrients and MTCT as well as other pregnancy-related outcomes.

- **Vitamin A**. Several studies have documented an association between vitamin A status and increased risk of MTCT but no studies have yet shown that vitamin A supplementation during pregnancy or post-delivery lowers this risk. For example, studies in Malawi found a positive association between maternal vitamin A deficiency and MTCT (Semba et al, 1994b), and subsequent infant (Semba et al, 1995) and maternal mortality (Semba, 1997). Kenyan studies also found that low serum retinol levels were associated with HIV levels in breastmilk and in vaginal secretions, suggesting that vitamin A status could influence transmission during delivery and through breastfeeding (Nduati et al, 1995).

  Several vitamin A supplementation trials have been carried out in Africa, although not all results have been published. Among the published studies, one trial in South Africa found that vitamin A and beta-carotene supplementation reduced the risk of pre-term deliveries but not MTCT of HIV (Coutsoudis et al, 1999a) (see Box, "Research Profile: South Africa—Vitamin A, MTCT, and Perinatal Outcome").

  Other trials in Tanzania studied the possible relationships between vitamin A supplementation and various outcomes for the mother and infant (see Box, "Research Profile: Tanzania—Multivitamin Supplementation, MTCT and Other Pregnancy Outcomes"). In terms of MTCT, it was found that vitamin A and multivitamin supplements did not reduce HIV transmission during pregnancy, nor during the intrapartum and early breastfeeding periods (Fawzi et al, 2000). The effect of the multiple micronutrient supplements on late postnatal transmission through breastfeeding is being studied.

  Randomized trials of vitamin A and other micronutrients during pregnancy were conducted in Malawi (vitamin A alone) and in Zimbabwe (multiple supplements) but results are not yet published. Another study, known as ZVITAMBO, is providing high-dose vitamin A supplements to mothers (400,000 IU) and/or babies (50,000 IU) within 96 hours of delivery. The study is following the mothers and babies prospectively to assess infant mortality, MTCT during breastfeeding, and incident HIV infection among the postpartum women. The study also provides HIV voluntary counseling and testing, including counseling on infant feeding options. ZVITAMBO will measure the impact of infant feeding counseling on feeding decisions and HIV disclosure practices.

RESEARCH PROFILE: SOUTH AFRICA

Vitamin A, MTCT, and Perinatal Outcome

Researchers in Durban, South Africa, observed that poor vitamin A status is associated with a higher risk of mother-to-child transmission of HIV and that evidence of the impact of vitamin A on other birth outcomes has been conflicting. This study was carried out to assess the impact of vitamin A supplementation on MTCT and other perinatal outcomes. A total of 728 pregnant women received either daily vitamin A (5000 IU retinyl palmitate and 30 mg beta-carotene) or a placebo during the third trimester of pregnancy. The vitamin A group also received 200,000 IU retinyl palmitate at delivery. There was no difference in MTCT rates at three months between the two groups (20.3 vs. 22.3 percent in the vitamin A and placebo groups respectively). Women receiving vitamin A were less likely to have pre-term deliveries (11.4 vs. 17.4 percent, $p < 0.03$). Within the pre-term group, those who received vitamin A were less likely to be HIV-infected (17.9 vs. 33.8 percent). The investigators conclude that although vitamin A did not reduce MTCT overall, supplementation may be effective in reducing pre-term births and HIV-infections in pre-term infants.

Source: Coutsoudis A, Pillay K, Spooner E et al (1999a).

ZVITAMBO has recently completed enrollment of 14,000 mother-baby pairs, who will be followed for up to 2 years (Humphrey et al, 2000).

- **Vitamin E.** Studies in Malawi (Semba et al, 1999a) and Kenya (John et al, 1999) have found that elevated breastmilk sodium levels (indicative of inflammation or infection) and clinical mastitis are associated with higher rates of postnatal transmission of HIV. Mastitis, or breast inflammation, has nutritional risk factors. Research conducted in Tanzania observed that intake of vitamin E was associated with rates of mastitis in breastfeeding women of unknown HIV status during the first 3 months post-delivery (see Box, "Research Profile: Tanzania—Vitamin E and Mastitis"). Selenium deficiency has also been implicated in increased incidence and severity of mastitis (Hogan et al, 1993), as have vitamin A and beta-carotene (Semba and Neville, 1999; Filteau et al, 1999b). Thus it appears that nutritional status may mediate the risk of HIV transmission through breastfeeding. It is not known, however, whether micronutrient supplementation (with vitamin E, selenium, vitamin A, or beta-carotene alone or in combination) may reduce mastitis-related HIV transmission.

In summary, to date, despite demonstrated associations between vitamin A deficiency and HIV infection, there is no evidence yet that vitamin A supplementation can positively alter HIV vertical transmission or disease progression in adults, including pregnant women. The impact of high-dose vitamin A supplements on late postnatal transmission has yet to be evaluated, although results from the ZVITAMBO and Tanzanian studies will help to answer this question.

Multiple micronutrient supplements, however, appear to have many beneficial impacts for offspring of HIV-infected women and may improve the immune status of postnatal HIV-infected women (see Box, "Research Profile: Tanzania—Multivitamin Supplementation, MTCT, and Other Pregnancy Outcomes"). However, the potential impact of these supplements in populations that are food insecure or consuming marginal to low levels of energy and protein are not known. Multi-micronutrient supplementation trials among uninfected women are being carried out in several countries to assess the benefits of multivitamin supplementation in the general population of pregnant women in developing countries (UNICEF, 1999).

E. Interpreting Research Studies

There are several methodological issues to consider when reviewing research on HIV/AIDS and nutrition conducted in non-African settings and when extrapolating these research findings to African populations. Fortunately, many

contributions in HIV and nutrition research have come from Africa. This is important because many of the studies conducted in the United States or other industrialized countries may not be directly relevant for African settings, for the following reasons:

- The general level of nutrition is higher in industrialized countries than in most of AIDS-affected Africa, where malnutrition is widespread. The impact of nutritional interventions usually depends on the underlying nutritional status of the individual being studied. If a nutritional supplement is given to correct a deficiency, it is more likely to have an impact than when it is given to persons who are nutritionally replete. Therefore, studies in the US and other industrialized countries may show no effect of nutrition (as a risk factor or as an intervention) on HIV outcomes, whereas an impact is, or could be, observed in Africa where malnutrition is common.

- Most studies of adults with HIV/AIDS conducted in industrialized countries have been among homosexual men and/or intravenous drug users. These two populations are likely to be different from each other in terms of diet, nutritional status, and health history. In addition, intravenous drug use may cause nutritional and/or metabolic alterations. Also, the diet, health status and behaviors, and nutritional status of homosexual men and intravenous drug users in industrialized countries are likely to be quite different from that of HIV-infected adults in Africa.

- Most American and European study subjects usually also have access to (and are taking) ARV drugs and other treatments for secondary infections, whereas similar therapies are rarely available to PLWHA in Africa. These drugs affect the course of HIV disease and some drugs have nutrient interactions. Although ARV use is generally controlled for during statistical analysis, study results may not be applicable in populations where ARV drugs and other therapies are not available. In addition, many American and European study participants also consume daily vitamin-mineral supplements and nutritionally fortified foods, whereas such supplements and fortified foods are not generally available or consumed by African PLWHA.

Studies of the relationship between nutrition and HIV also vary greatly in design as well as in the variables being measured. Some important considerations are described:

- Whereas some studies have investigated relationships between *intakes* of micronutrients and HIV status, others have investigated relationships between micronutrient *status* (usually reported as serum or plasma levels) and HIV. Care must be taken when using blood levels to measure the micronutrient status of people with acute infections. Serum concentrations of several nutrients (e.g., iron, zinc, retinol/vitamin A) decline during the acute phase response, either because they are redistributed in the body or because they are bound to acute phase proteins. Thus, the level of the nutrient in the blood may be a poor

RESEARCH PROFILE: TANZANIA

Vitamin E and Mastitis

Mastitis causes junctions in the mammary epithelium to become "leaky," enabling blood plasma constituents (e.g., HIV) to enter breastmilk. Mastitis may be due to infectious agents, or caused by poor positioning or weak suckling, resulting in breast engorgement. Cytokines and other immune reactions resulting from mastitis can damage the intestines of very young babies. Elevated breastmilk sodium is a marker for mastitis. Studies suggest that deficiencies of vitamin E and selenium, two anti-oxidants, may increase risk of mastitis. A randomized trial conducted in Tanzania provided breastfeeding women with dietary advice and either red palm oil with 2 mg provitamin A and 1 mg of vitamin E or sunflower oil with 5.7 mg of vitamin E. A control group received only dietary advice and 4 kg of rice per month for their family. Results showed that women consuming the vitamin E-rich sunflower oil had lower rates of mastitis than women in the control and red palm oil groups.

Source: Filteau SM, Lietz G, Mulokoze G et al (1999a).

indicator of actual nutrient status, potentially causing misclassification of nutritional status (Fawzi and Hunter, 1998).

- Many studies also show a weak correlation between dietary intake and blood levels of the same nutrients, which could lead to the conclusion that increasing intake of the nutrient might not improve nutrient status. However, the weak correlation may be due to poor reliability or inaccuracy of the intake measurements (due to poor recall or daily/monthly variation in food consumption), or it could result from the phenomenon described above where nutrient concentrations in blood samples are lowered during infection. It is important to take note of the methods used to measure dietary intake when interpreting and comparing studies.

- The possibility of "reverse causality" must always be considered when interpreting observational studies of HIV/AIDS and nutrition. That is, it is often likely that HIV disease has resulted in reductions in nutrient intakes, blood levels, and status, rather than the reverse, that reductions have caused a worsening of disease. In some cases, knowledge of HIV status may also result in changes in dietary practices (or supplementation use) which may further complicate interpretation, as recent diet may not reflect longer term dietary patterns or nutrient stores. For these reasons, randomized intervention trials are best suited for learning about how nutritional interventions may impact HIV/AIDS outcomes (Fawzi and Hunter, 1998). Unfortunately, relatively few nutrition intervention trials have been carried out among PLWHA in industrialized or developing countries.

- Some studies have assessed the association between individual nutrients (e.g., vitamin A alone) and HIV outcomes, whereas others have taken into account (or provided) multiple nutrients. The impact of single nutrient interventions, as noted previously, may be attenuated when deficiencies of other nutrients are present, and findings in one population may not apply to another population with a different nutritional profile. In addition, intakes and status of vitamins and minerals tend to be highly correlated with each other (since all foods contain many different micronutrients). This makes it difficult to distinguish the role of individual nutrients in statistical analyses, and can result in erroneous conclusions about the importance of one nutrient that has been measured over another that has not been directly measured but is highly correlated with the one that has.

- Studies have used a variety of different variables to characterize HIV status, making comparisons between studies complicated at times. For example, some researchers have looked for associations between micronutrient status and CD4 cell counts, whereas others have looked at disease progress measured by time to specific symptoms or death. Both indicators are used to describe HIV disease progression.

- Studies vary greatly in their length of follow-up, which could affect comparisons and bias conclusions.

- Not all investigators have controlled for disease or nutritional status at the time of enrollment, making it difficult to disentangle the effects of the infection on nutrition from the nutritional risk factors for disease outcomes.

- Some studies measure changes in body weight following nutritional interventions whereas others have measured body cell or lean body mass. Measuring changes in body weight is less than optimal, and can be misleading, because weight gain or stabilization can occur in the presence of muscle wasting when feeding interventions increase body fat and water only.

- Finally, studies of HIV/AIDS and nutrition do not always measure important behaviors, such as alcohol use, which could affect disease progression as well as nutrition.

These differences in study populations, study design, and methodology have made it difficult to extrapolate findings from one population to another and to draw practical lessons for African nutrition or HIV programs from available research. In summary, the relationship between HIV/AIDS and nutrition involves several complex biological processes. Both malnutrition and HIV/AIDS directly affect the immune system, impairing people's ability to resist and fight infection. Nutrition interventions to prevent or reverse

weight loss and wasting associated with HIV infection may help to preserve independence, to improve quality of life, and to prolong survival. Micronutrient interventions may help to strengthen the immune system and reduce the severity and impact of opportunistic infections in PLWHA. Some nutritional imbalances may directly affect HIV viral replication. Correcting these imbalances may also help to slow HIV disease progression and prolong survival.

IV. Nutrition Support for People with HIV and AIDS

A. Introduction

Many of the programs in Africa that offer nutrition support for PLWHA demonstrate an enormous commitment by health staff and other community providers to provide holistic care in a community-based, realistic, and sustainable way. This nutrition support is often offered in a context of extreme deprivation, economic hardship, social stigma, endemic malnutrition, and food scarcity. Many of the persons providing nutrition support are devoted volunteers whom themselves have been personally affected by the direct or indirect effects of the AIDS epidemic in their communities.

These extraordinary hardships have prevented most African nutrition programs that serve PLWHA from being rigorously evaluated. Even so, they have, according to informal reports, resulted in a significantly increased quality of life and, perhaps, survival of the patients concerned. In addition, anecdotal evidence points to a number of difficult-to-measure yet important benefits for people living with HIV or already affected by AIDS, such as experiencing improved independence, greater control over the progress of their illness, and peaceful and dignified death as a result of these efforts.

A complete review of programs and educational materials for nutrition support for PLWHA in Africa has recently been conducted by FAO, and readers interested in a complete description of these should consult Bijlsma (2000). Some examples of African nutrition support programs for PLWHA are described below. The programs have activities that range from providing dietary advice for "positive living" to developing and testing recommendations for palliative care for people who are already suffering from the symptoms and infections that accompany full-blown AIDS. Other programs provide food and home-based care to AIDS patients and their families. Some programs have developed and/or recommended a wide range of local herbal remedies, which they believe to be beneficial, although most have not been evaluated scientifically to test their efficacy.

Clearly this summary is not representative of all the efforts currently being undertaken in Africa. However, because most programs are home and/or community-based, frequently with little or no external support, there is limited published literature available to include in a review of this type.

- **Kenya.** The Association of People with AIDS in Kenya (TAPWAK) developed nutritional guidelines for people with AIDS-related conditions such as diarrhea, weight loss, digestive problems, and mouth sores. A review of the literature and practical experience (conducted by TAPWAK) identified specific local herbs and spices that were found to be useful in reducing digestive problems, colds, and flu, and could be recommended for people with AIDS-related symptoms. TAPWAK members following this advice reported that they were able to control diarrhea, maintain weight, and have a sense of controlling their own health (Awour et al, 1998).

- **Nigeria.** In Nigeria, a community-based, home-delivered meal program was set up to meet the specialized nutrition needs of homebound people with AIDS. Home-based nutritional support and care has many advantages over similar care offered in hospitals. An evaluation of this project revealed that the home-based approach cost only 38 percent of what a 90-day hospital stay would cost. In addition, patients receiving home-based nutrition support had greater choice over the foods that they ate and could also enjoy their meals in a familiar setting (Fakande and Malomo, 1998).

- **Zambia.** The AIDS Department of the Ndola Catholic Diocese initiated a home-based care program in 1991 to provide basic nursing and medical care to people with AIDS and to provide emotional, social, and spiritual support to patients and family members affected by the disease. The program works through community organizations and uses volunteers as its front-line workers. The program provides maize meal, a high-energy protein supplement,

beans, cooking oil, and salt to families affected by AIDS, including orphan caregivers. The families pay a small cash contribution of about 10 percent of the retail value of the food to help support the program. However, destitute families may receive food free of charge. Other services provided include practical help caring for sick patients, counseling by nurses and volunteers, and information dissemination to dispel misconceptions about HIV/AIDS. The impact of the program has not been fully assessed, but one review found that the cost of the program was less than US$1 per person served. This compares favorably with the expenses of families who have to pay for transport and other hospitalization costs (Blinkhoff et al, undated).

- **Zimbabwe.** A group called "The Centre" counseled over 600 clients between 1992 and 1998, teaching them basic nutrition practices using traditional foods. The program includes educational messages that describe which foods contain vitamins and minerals, and how these foods can be prepared and presented. The Centre reports that their nutrition counseling has helped many PLWHA to return to a productive lifestyle (Francis, 1998).

In addition to these programs, several organizations, including the African Network of People with HIV/AIDS (e.g., Ndiaye, 1997; Epstein, 1995) as well as local health departments (e.g., Bijlmsa, 1996), have developed nutrition and dietary guideline booklets for PLWHA. These booklets usually include food preparation instructions (to minimize contamination) and recipes utilizing local foods for people suffering from different digestive problems and symptoms, such as diarrhea, candidiasis, and nausea. The content of these booklets has been reviewed in Bijlsma (2000). While most of the information contained in these guidelines is accurate and useful, the benefits of some recommendations, particularly related to the therapeutic uses of different foods, herbs, and spices remain unsubstantiated. A review of the benefits and potential risks of non-traditional food-related therapies for strengthening the immune system of PLWHA is beyond the scope of this review. The remainder of the chapter, however, will provide practical, evidence-based advice for nutritional support for PLWHA based on the literature reviewed earlier and experience in clinical nutrition.

B. Nutritional Support Program Options

The goals of a program to provide nutrition support for PLWHA may vary from *prevention* of nutritional depletion among people who are HIV-positive to the provision of *palliative nutrition care and support* for people with AIDS and for the families who care for them. Specific objectives for such programs include to:

- improve or develop better eating habits and diet among people with HIV/AIDS;
- build or replenish body stores of micronutrients;
- prevent or stabilize weight loss;
- preserve (and gain) muscle mass;
- prevent food-borne illness;
- prepare for and manage AIDS-related symptoms that affect food consumption and dietary intake; and
- provide nutritious food for AIDS-affected families living in conditions of food insecurity (Abdale and Kraak, 1995).

Nutritional support for people with HIV and with AIDS should be provided in a holistic manner. Other components of care that should be provided include appropriate treatment of opportunistic infections; stress management; physical exercise; and emotional, psychological, and spiritual counseling and support (Abdale and Kraak, 1995). Proper nutritional support may prevent weight loss associated with opportunistic infections; speed recuperation from HIV-related infections; prevent diarrhea and other digestive discomforts associated with fat malabsorption; and allow PLWHA to participate directly in their own care (Awour et al, 1998; Abdale and Kraak, 1995).

Programs that provide nutritional care and support may include one or more of the following components:

- nutrition education and counseling in health facilities, in community settings, or at home to change dietary habits, to increase consumption of key foods and nutrients, or to manage anorexia and other conditions that affect eating patterns;

- water, hygiene, and food safety interventions to prevent diarrhea;

- food-for-work programs for healthy family members affected by HIV/AIDS, including orphan caregivers;
- food baskets for home preparation; and
- home-delivered, ready-to-eat foods for home-bound AIDS patients who are unable to prepare their own meals.

Although it is well recognized that the social and food security context of the entire family affected by HIV/AIDS must be considered when designing nutrition support programs, the following section of the paper will specifically focus on recommendations for nutrition counseling and care of PLWHA.

C. Recommendations for Nutrition Care and Support for Adults with HIV and AIDS

Recommendations for nutrition counseling and care for people with HIV/AIDS vary depending on the underlying nutritional status of the individual and the stage of infection or level of disease progression. Advice provided during the early (asymptomatic) stages of infection will focus on maintaining health and building nutrient stores; during the middle stages of the disease emphasis may shift to managing problems associated with anorexia, acute infections (lasting less than 2 weeks), and malabsorption of fat and related nutrients. Once secondary infections become chronic, and infection-induced changes in metabolism cause protein catabolism and wasting-related symptoms, nutritional support will be oriented toward mitigating the adverse nutritional effects of chronic diarrhea and other secondary infections, and recuperative feeding during periods when symptoms have subsided. Nutritional support is likely to be more effective at promoting well-being, independence, and quality of life if it is provided at the early stages of the infection rather than only during later stages of the disease (Stack et al, 1996).

Nutrition support has become increasingly sophisticated for persons with HIV and AIDS in industrialized countries. This support begins with early diagnosis of HIV infection, and it includes frequent measurements of body composition (assessment of fat and fat-free body mass and/or body cell mass); serum and other tests to measure micronutrient levels; oral nutrition supplements (including multivitamins and high-protein and energy drinks); and appetite stimulants (Walsek et al, 1997). Non-volitional feeding through enteral (by mouth or feeding tube) or parenteral therapy (by intramuscular or intravenous injection) may also be provided at later stages of disease. While treatment for AIDS wasting in industrialized countries has been greatly improved with the use of hormones and appetite stimulants, these are prohibitively expensive and not likely to be available in most African settings.[5]

In Africa, early detection of HIV is rare due to the absence of systematic screening or voluntary counseling and testing services for persons at risk. As a result, assessment of nutritional status usually begins when the patient appears with symptoms of AIDS. This assessment is often limited to measurement of body weight or arm circumference to assess physical wasting and a dietary assessment. Treatment most commonly involves, at best, provision of nutritious food supplements and/or counseling on improved eating habits.

Although most health systems and community support structures in Africa have limited capabilities for comprehensive nutrition assessment and support services, the preceding review has yielded some principals and guidelines that can be applied within existing programs in resource poor settings. These are summarized below.

1. Recommendations for nutritional support for HIV-positive, asymptomatic individuals

- A healthy diet that is adequate in terms of energy, protein, fat, and other essential nutrients, should be promoted as a key component of positive living for people with HIV. Good nutrition and a healthy diet may help prolong the period of time between HIV infection and the onset of secondary infections commonly attributed to progression to AIDS. This is because of the relationship between nutritional status and immune system function and integrity described in Chapter III. Knowing that

[5] For example, an analysis of the annual cost of treatments for patients with AIDS wasting (Corcoran and Grinspoon, 1999) showed that nutritional supplements and appetite-stimulating drugs can vary from US$2200 (for Dronabinol) to US$3200 (for Megestrol acetate). The cost of testosterone and testosterone analogues can reach over US$10,000. The cost of recombinant human growth hormones alone can reach up to US$36,000. A less expensive option of glutamine plus antioxidant vitamins (US$1600) was discussed in Chapter III.C.

there are actions that HIV-infected people can take to improve the quality, economic productivity, and longevity of their lives may also be an important incentive to getting an HIV test before serious symptoms of AIDS appear.

- As noted earlier, nutrition counseling and support should be part of a larger health promotion and holistic support program for PLWHA. Algorithms for the nutritional management of people with HIV/AIDS should be developed, and appropriate locally available foods should be identified. All health and support personnel who counsel and/or provide medical care to PLWHA should be familiar with these algorithms and foods. Home-based care providers should be familiar with the basic nutritional advice and practices for the patients they care for. They also need to access local sources of social support which might exist to help address problems of household food security for families affected by HIV/AIDS.

- Nutrition counseling should include information on locally available foods and diets to meet estimated requirements given the individual's age, sex, and physiologic state (e.g., pregnancy, lactation, engaged in strenuous physical labor, etc.). It is important to recognize that people with HIV, even if they are asymptomatic, may have increased body metabolism, which increases their daily energy, protein, and micronutrient requirements (Macallan, 1999b; Macallan, 1999c; Woods, 1999). This is due to the immune and endocrine response that occurs with all infections, even sub-clinical ones, described in Chapter III. Although the evidence is not conclusive, at early stages of infection an individual's ability to develop nutritional reserves is likely to be greater than at later stages. Therefore it is suggested that people with asymptomatic HIV try to increase their daily energy and protein intake to meet these increased requirements.

- Based on existing studies, it is recommended that HIV-positive adults increase their energy intakes by about 10-15 percent, to about 40 kcal/kg body weight, to maintain their weight, and somewhat more (50 kcal/kg) to actually gain weight (Woods, 1999). This amounts to an additional 300 to 400 kcal/day for adult women and men, respectively, for weight maintenance. Protein intake should also be increased to protect lean body mass, with recommended levels reaching about 1.5 g/kg body weight, or a 50 percent increase (Woods, 1999). In real terms this amounts to about 25-30 additional grams of protein/day in adults. These energy and protein increases can be realized by consuming high-energy, high-protein snacks twice or three times daily, such as a cup of yogurt, dried fish, or peanut butter on bread, with milk (fermented or fresh).

- Although not discussed in detail in this paper, people living with HIV should be encouraged to maintain their levels of physical activity. Weight-bearing exercise may be helpful in building lean body mass, and exercise may also help to stimulate appetite.

- Information presented in Chapter III highlights the important role of antioxidants (e.g., vitamins E, C, beta-carotene, selenium) and B-vitamins for preserving immune function and delaying disease progression. In light of this, care should be taken to select dietary items that are rich in these micronutrients (see **Table 3**). Unfortunately, the studies reviewed in Chapter III suggest that PLWHA may need to consume 2 to 5 times the recommended daily allowance[6] of these nutrients for healthy individuals (or more for vitamin E) in order to delay HIV progression. Although food sources are generally preferred, it is likely that daily multiple vitamin-mineral supplements will be needed to reverse underlying nutrition deficiencies and build the nutrient stores of people with HIV in Africa. Any supplement that is recommended should contain the antioxidants and B-vitamins mentioned above; caution is advised with respect to zinc and iron supplements (see Chapter III).

  It is important to point out that the efficacy of multiple micronutrient supplements for delaying HIV disease, and the impact of supplementation among HIV-infected individuals with chronically low energy and protein intakes are still unknown. There is no basis for recommending daily, high-dose micronutrient

[6] It is recognized that countries may have their own recommended intakes and allowances, which need to be considered when developing locally specific feeding messages. However, the RDAs published by the National Academy of Sciences (1989) are referred to here because most studies reported intakes relative to these allowances.

supplements (e.g., containing more than 5 times the RDA). Excess intake of many micronutrients may actually reduce immune responses (Chandra, 1997).

In addition to these general guidelines, counseling should include discussion of hygiene and safe food handling and preparation of all items that are consumed, particularly given increased susceptibility of HIV-infected individuals to bacterial infections. Failing to prevent contamination can result in diarrhea, which could have spiraling nutrition and health consequences for the HIV-infected. Hygiene and food safety messages should include these practices:

- Always wash hands before food preparation and eating and after defecating.
- Keep all food preparation surfaces clean and use clean utensils to prepare and serve foods.
- Cook food thoroughly.
- Avoid contact between raw foodstuffs and cooked foods.
- Serve foods immediately after preparation and avoid storing cooked food.
- Wash fruits and vegetables before serving.
- Use safe water that is boiled or filtered.
- Use clean cups and bowls, and never use bottles for feeding babies.
- Protect foods from insects, rodents, and other animals.
- Store non-perishable foodstuffs in a safe place (separate from pesticides, disinfecting agents, or other toxic chemicals).

In all cases, PLWHA should be encouraged to seek immediate attention for any digestive and health-related problems in order to prevent further nutritional and physical deterioration.

2. Recommendations for nutritional support for HIV-positive individuals experiencing weight loss

- If weight loss has already occurred, providers should try to ascertain the circumstances surrounding this. Research suggests that most early weight loss associated with HIV/AIDS occurs episodically, as the result of depressed appetite during secondary infections (Macallan, 1999c). Therefore, specific advice on how to maintain intake during these periods, (e.g., through more frequent meals and snacks and through the consumption of well-liked foods), should be provided. Following periods of appetite loss, fever, or acute diarrhea, people with HIV should try to increase intake to promote nutritional recovery. The recommendations above (in subsection C.1.) apply at this time; however, greater attention must be paid to minimizing the nutritional impact of infection. **Table 4** contains nutrition advice for managing common conditions.

- All PLWHA should be advised to avoid unhealthy lifestyles that include alcohol consumption, tobacco and drug use, which affect many nutritional processes, and unsafe sexual practices, which increase risk of re-infection or co-infection with HIV and other sexually transmitted diseases. PLWHA should be advised to seek medical attention as early as possible to treat any secondary infections that may arise (e.g., mouth sores, skin infections, cough, fever, diarrhea, tuberculosis). Counseling should emphasize that good nutrition and a healthy lifestyle today can help to preserve health, improve quality of life, and prolong independence as well as focusing solely on lengthening survival (Gorbach et al, 1993).

3. Recommendations for nutritional support for people with AIDS

Nutritional advice for persons suffering common AIDS-related symptoms (e.g. chronic diarrhea, mouth sores, fevers, chills, chronic cough, and wasting) is similar to what has been described above except that the emphasis shifts from preventing to mitigating the nutritional consequences of the disease and to preserving functional independence wherever possible. Consideration should also be given to the nutritional consequences of various drugs that AIDS patients may be taking.

The following points should be taken into consideration and followed by people with AIDS and by their caregivers (Abdale and Kraak, 1995):

- Preservation of lean body mass remains important at this stage, and earlier recommendations regarding energy and protein consumption should be maintained as long and as often as possible.

- During periods of nausea and vomiting, people with AIDS should try to eat small snacks throughout the day and avoid foods with strong or unpleasant aromas. Fluid intake must be maintained to avoid dehydration.

TABLE 4. Practical Suggestions on How to Maximize Food Intake During and Following Common HIV/AIDS-related Infections

Symptom	Suggested strategy
Fever and loss of appetite	Drink high-energy, high-protein liquids and fruit juice Eat small portions of soft, preferred foods with a pleasing aroma and texture throughout the day Eat nutritious snacks whenever possible Drink liquids often
Sore mouth and throat	Avoid citrus fruits, tomato, and spicy foods Avoid very sweet foods Drink high-energy, high-protein liquids with a straw Eat foods at room temperature or cooler Eat thick, smooth foods such as pudding, porridge, mashed potato, mashed carrots or other non-acidic vegetables and fruits
Nausea and vomiting	Eat small snacks throughout the day and avoid large meals Eat crackers, toast, and other plain, dry foods Avoid foods that have a strong aroma Drink diluted fruit juices, other liquids, and soup Eat simple boiled foods, such as porridge, potato, beans
Loose bowels	Eat bananas, mashed fruits, soft rice, porridge Eat smaller meals, more often Eliminate dairy products to see if they are the cause Decrease high-fat foods Don't eat foods with insoluble fiber ("roughage") Drink liquids often
Fat malabsorption	Eliminate oils, butter, margarine, and foods that contain or were prepared with them Eat only lean meats Eat fruit and vegetables and other low-fat foods
Severe diarrhea	Drink liquids frequently Drink oral rehydration solution Drink diluted juices Eat bananas, mashed fruits, soft rice, porridge
Fatigue, lethargy	Have someone pre-cook foods to avoid energy and time spent in preparation (care with re-heating) Eat fresh fruits that don't require preparation Eat snack foods often throughout the day Drink high-energy, high-protein liquids Set aside time each day for eating

Adapted from Woods (1999).

- To minimize gastrointestinal discomfort, gas, and bloating, foods that are low in insoluble fiber and low in fat should be consumed. If there is lactose intolerance, milk and dairy products should be avoided. Caregivers should try to identify fermented or non-dairy, high-protein foods that are easy to prepare and consume. Spicy foods should be avoided.

- During diarrhea, ensure that fluid intake is maintained (30 ml/kg body weight per day for adults and somewhat more for children). Patients should continue eating and drinking whenever possible and oral rehydration solution should be given to avoid life-threatening dehydration.

- For people with mouth and throat sores, hot and spicy or very sweet foods should be avoided, as should caffeine and alcohol. Patients should be encouraged to eat preferred (favorite) foods that are softened, mashed, or liquefied, if necessary.

- For patients with depressed appetites or lack of interest in eating, caregivers should try to increase dietary intake by offering small portions of food several times a day. Specific eating times should be set, and caregivers should try to find ways to make eating times pleasant and supportive.

- All infections that affect appetite, ability to eat, and nutrient retention should be treated immediately.

- Tobacco products should be avoided.

- The guidelines given previously for hygiene and food safety should be followed.

Several medications given to treat opportunistic infections have nutritional consequences, either because of drug-nutrient interactions or because side effects such as nausea and vomiting affect the intake and retention of nutrients. Practitioners who are prescribing these drugs must also ensure that nutritional consequences are addressed so that the patient is not disadvantaged further by AIDS-related therapeutic treatments. For example:

- Vitamin B_6 should be administered with isoniazid therapy for TB to avoid Vitamin B_6 deficiency (CDC, 1998a).

- Iron and zinc-containing supplements should not be taken with ciproflaxacin (take at least 2 hours apart) (Thomas, 1995).

- Many antiretroviral drugs have dietary requirements (e.g., to be taken on an empty or full stomach) and most have side effects such as nausea, vomiting, abdominal pain, and diarrhea, which must be managed nutritionally. Some drugs, such as ZDV, affect red blood cell production and increase the risk of anemia (CDC, 1998b).

Finally, when considering overall nutrition support for PLWHA in situations of food insecurity, efforts to secure basic foods for families should be made, where possible. However, caution is advised in the use of food donations. If food aid is given, care should be taken to ensure that these foods complement rather than replace the foods normally consumed by the patient. In designing such regimens, one must be aware of the food and nutritional situation of the patient's family. Often, as noted in the introductory sections of the paper, a family caring for a person with HIV/AIDS in Africa is extremely vulnerable and likely to be food insecure. A food ration is likely to be shared or handed over completely to other family members, including children. Therefore, it is preferable for food supplements to be of sufficient size to meet the needs of the HIV/AIDS patient and his/her dependents, if resources permit. It is also recommended that counseling be given to the patient as well as his/her caregivers on how the supplement should be prepared and offered to maximize food safety and appropriate consumption by the person with HIV/AIDS.

D. Recommendations for Nutrition Care and Support for Children with HIV/AIDS[7]

Children of mothers who are HIV-infected are especially vulnerable to malnutrition and mortality, either as a result of their own HIV infection if acquired from their mother, or because of the deteriorating health of one or both parents. Therefore, it is important that all children born to HIV-infected mothers receive well-baby care and

[7]At present, there are no specific guidelines on the nutritional management of children with HIV and AIDS available from WHO or UNAIDS. The recommendations contained in this section are likely to be modified and expanded on as new information becomes available and consensus on nutritional care and support for HIV-infected children is reached.

have their growth monitored regularly. This is especially important for babies who are not being breastfed and for those who have been weaned early. Failure to gain weight may be a sign of HIV-infection or other health problems, or it could reflect inadequate feeding practices.

Specific nutritional recommendations for children with HIV should follow the recommendations for all young children, taking into consideration the increased nutritional requirements that accompany the infection and the increased likelihood of fat and other nutrient malabsorption discussed in Chapter III. It is also important to remember that young children (i.e., less than 2 years old) need to be fed patiently and persistently, with supervision and love. This is especially true for HIV-infected children who may be frequently ill and suffering from fever, mouth and throat sores, and depressed appetite.

Solid foods should be introduced gradually to match the age and developmental characteristics of the child. First foods should be soft and enriched with energy sources (e.g., oil, peanut butter, sugar, etc.). Small portions (200-250 ml) should be fed frequently (at least three times per day) because the young child's stomach is small. The size of the portion should be increased as the child gets older. Most children, by the time they are 1 year old, can eat all the foods of the adult diet, except those that are very spicy, as long as they are cut, mashed, or ground to prevent choking. However, care must be taken to ensure that the young child's diet contains as much variety as possible to prevent diet monotony and to increase intake of essential vitamins and minerals. Caregivers should feed children a variety of locally available fruits and vegetables, and animal products and fortified foods, if they are available. Nutritious snacks (e.g., fruit, bread) can be provided between meals during the day to increase consumption. Daily multi-nutrient supplements, if available, may be helpful in preventing nutritional deficiencies (see Chapter III. D).

In addition to solid foods, children who are not breastfed require non-human milks in their diet for at least the first year of life and preferably longer (Savage King and Burgess, 1995). Non-breastfed children are likely to be at the highest risk for malnutrition. Additional information on HIV and infant feeding is found in Chapter V.

The same recommendations offered to adults for following safe and hygienic practices, and for feeding during and following acute infections also apply to children. The feeding recommendations in **Table 4** can be followed for the nutritional management of specific symptoms and conditions.

Guidelines for the nutritional management of HIV-infected children have been suggested by Lepage (Lepage et al, 1998) and others. They include:

- Body weight, height, arm circumference, and triceps skin fold should be monitored regularly.

- The child's diet should be reviewed at every well-child and sick-child health visit. Conditions affecting appetite and food intake should be discussed and treated, as appropriate. Advice on how to improve the diet should be given, taking into consideration the child's age, local resources, and the family circumstances.

- HIV-infected children should be immunized and given periodic prophylactic vitamin A supplements, according to local immunization and vitamin A guidelines.

- For children with secondary infections, such as tuberculosis, oral thrush, persistent diarrhea, and pneumonia, prompt treatment is important. The nutritional impact of these infections should be minimized by maintaining food and fluid intake to the degree possible (see **Table 4**) and by increasing intake after the acute symptoms have subsided.

- Many HIV-infected children are likely to become severely malnourished. Local guidelines for the management of severe malnutrition should be followed (e.g., WHO, 1999). Enteral or parenteral nutrition should be considered, when available, if the child is unable to eat.

V. HIV and Infant Feeding: A Research and Program Update

A. Introduction

Since the mid-1980s, when HIV was first detected in breastmilk and cases of HIV transmission to infants during breastfeeding were documented, policy makers and program managers in Africa have struggled to develop appropriate guidelines on infant feeding for mothers who are infected with the virus. Even today, decisions about infant feeding in settings of high HIV prevalence require a careful balancing of risks, with the risk and fear of transmitting HIV through breastfeeding on one side, and the risk and fear of mortality, morbidity, and stigmatization that can result from not breastfeeding on the other. Unfortunately, there are few studies with data on the risks of artificial feeding in African settings because breastfeeding is nearly universal in Africa, making balancing of risks especially challenging (Latham and Preble, 2000).

The issue of appropriate infant feeding practices in populations with high HIV prevalence rates is particularly important in sub-Saharan Africa because:

- rates of HIV in pregnant women are high and rising dramatically;
- nearly all African women initiate breastfeeding at birth and the duration of breastfeeding is often greater than 24 months (yet the introduction of water and watery gruels generally occurs early, within the first 3 months of life);
- the nutritional, immunologic, psychological, birth-spacing, and other benefits of breastfeeding are especially important in resource-poor settings; and
- the alternatives to breastfeeding in many African settings are unsafe and usually unaffordable.

In general, infants who are not breastfed in developing countries have higher rates of childhood illness, malnutrition, and mortality than breastfed infants (WHO, 2000; Latham, 1999). This is due to the high cost and, often, irregular supply of breastmilk substitutes; the lack of safe clean drinking water with which to mix commercial or home-prepared milk formula; and to limited supplies of fuel for boiling water.

A recent pooled analysis from research undertaken in Brazil, Pakistan, and the Philippines found that babies who were not breastfed were 5.8 times more likely to die in the first month of life than breastfed babies. The survival protection afforded by breastfeeding declined with age but was significant through the first 8 months of infancy. The impact of breastfeeding on child survival was greatest among mothers with limited education, suggesting that the benefits of breastfeeding in some African settings will be even greater than these numbers suggest (WHO, 2000).

A study carried out in Nairobi, Kenya (described in greater detail in Section B), found that mortality rates at 24 months were not significantly different between breastfed (24 percent) and formula-fed (20 percent) babies born to HIV-positive mothers (Nduati et al, 2000b). Consistent with the pooled analysis, the formula-fed infants were more likely (5 percent) than the breastfed infants (0.8 percent) to die in the first 6 months of life (Mbori-Ngacha et al, 2000).

As the risk of HIV transmission through breastfeeding becomes more widely understood, HIV-infected African women face the difficult burden of having to decide whether to break with tradition and choose not to breastfeed, or breastfeed and run the risk of infecting their infants with HIV. The decision not to breastfeed comes with its own social risks, including the stigma or suspicion of being infected with HIV — a risk that sometimes carries grave social, emotional, and physical consequences. In an attempt to minimize risks to her infant, yet hide her own status from neighbors, friends or family, an HIV-infected mother may combine breastfeeding with artificial feeding — the worst of all possibilities as it exposes the infant to both sets of risks.

In mid-1998, three UN agencies released guidelines on HIV and infant feeding for decision makers, and for health care managers and supervi-

sors (UNICEF et al, 1998a; 1998b). For the first time, the recommendation to provide HIV-positive mothers who decide not to breastfeed with replacement feedings was formally introduced by these organizations. Replacement feeding options include the use of commercial infant formula; home-prepared infant formula; modified full-cream powdered milk formula; and modified breastfeeding practices, such as feeding an infant on expressed and heat-treated breastmilk or early cessation of breastfeeding. After 6 months, general information on feeding with home-prepared foods is provided.

These guidelines on HIV and infant feeding are generic and should be adapted to local circumstances. Their application through counseling must be tailored to the specific circumstances of individual women. Several countries in Africa have begun to develop and implement local guidelines for HIV and infant feeding. However, it is not known whether these guidelines are being implemented effectively and what, if any, impact they are having on infant feeding decisions. A recent study conducted in Zambia (see Box, "Research Profiles: Zambia—HIV and Infant Feeding Options") illustrates some of the challenges of ensuring safe replacement feeding in a poor African setting (Piwoz et al, 1999).

B. HIV Transmission through Breastfeeding

The mechanisms by which HIV is transmitted through breastfeeding are not precisely understood. HIV is present in cells and in cell-free components of breastmilk of infected mothers. Infants may become infected with HIV if the consumed virus enters their intestinal mucosa through a breach in the integrity of the epithelial layer (e.g., from trauma due to the introduction of food antigens and pathogens); through small defects in the junctions between epithelial cells resulting from nutritional deficiencies; or with other pathogens (Van de Perre, 1999). Other, as yet undefined, mechanisms of infection are also possible.

Over the past decade, many studies have been carried out to improve our understanding of the HIV-breastfeeding relationship, to better understand the risk factors for HIV transmission through breastfeeding, and to identify ways to make breastfeeding safer in HIV-infected mothers. Much of the early work on HIV and breastfeeding came from studies in Rwanda, which estimated the risk of postnatal transmission (Van de Perre et al, 1991); made the first link between postnatal transmission and breast abscesses (Van de Perre et al, 1992); investigated infective and anti-infective properties of breastmilk in HIV-infected women; and identified an association between defective IgM response against HIV and increased risk of infection in breastfed infants (Van de Perre et al, 1993).

A number of factors have now been identified which appear to increase the risk of HIV transmission through breastfeeding (see **Table 5**). These include maternal viral load and virus type and other viral characteristics; maternal immune status; breastfeeding duration; the type of breastfeeding practiced (babies who are breastfed exclusively with no other early introduction of solid foods or other liquids appear to have lower risks of HIV transmission than mixed-fed infants); and the presence of breast abscesses, mastitis, cracked nipples, and oral lesions in the infant (UNICEF et al, 1998c).

Since the early and mid-1990s, the role of breastmilk in HIV transmission has been the subject of increased study. A thorough review of the literature is beyond the scope of this paper. Readers interested in more detailed information are referred to Preble and Piwoz (1998), UNICEF et al (1998c), and de Cock et al (2000). Below is a summary of the highlights of recent studies and analyses on breastfeeding-related HIV transmission.

- **Exclusive breastfeeding.** This term refers to breastfeeding without supplementary feeds such as water, other liquids, or semi-solid foods. In general, exclusive breastfeeding is recommended for the first 6 months of life. Exclusive breastfeeding reduces the risks of infant mortality from diarrhea and respiratory infections (Victora et al, 1987; 1989), and it also protects against other diseases, such as neonatal sepsis, acute otitis media, and necrotizing enterocolitis (Piwoz, 2000).

  A study in Durban, South Africa (Coutsoudis et al, 1999b), observed that infants of HIV-positive mothers who were breastfed for at least 3 months (n=103) had a significantly lower HIV transmission risk by 3 months (14.6 percent) than did those who also received other fluids or

TABLE 5. Risk Factors for HIV Transmission through Breastfeeding and Strength of the Evidence Related to Vertical Transmission

Risk factor	Strength of the evidence
High maternal HIV viral load - recent infection - advanced disease	strong
Advanced disease - clinical symptoms	strong
Immune deficiency - low CD4 - high CD8 cell counts	strong
Maternal malnutrition - vitamin A deficiency	limited
Duration of breastfeeding	strong
Non-exclusive breastfeeding in first 3-6 months	limited
Breastfeeding while experiencing breast infections - mastitis, abscesses	strong
Breastfeeding while experiencing nipple fissures	strong
Breastfeeding an infant with mouth sores	limited

Adapted from UNICEF et al (1998c).

foods in early infancy ("mixed-breastfeeding"; 24.1%; n= 288; p< 0.03). This represents a 48 percent reduction in transmission risk, after adjusting for potentially confounding variables. The MTCT rate for exclusively breastfed and never breastfed infants was similar through the first 6 months (about 20%). At 15 months, 24.7 percent of the babies who had been exclusively breastfed for at least three months were HIV-positive, compared to 35.9 percent of the mixed-fed babies (Coutsoudis, 2000). Infant mortality was also greater among the mixed-fed (15 deaths) and formula-fed (7 deaths) babies. None of the infants who were exclusively breastfed died during the follow-up period. These findings suggest that exclusive breastfeeding followed by early and abrupt weaning may be one option for reducing MTCT through breastfeeding while minimizing the adverse consequences of replacement feeding in Africa, according to the researchers. Further studies on exclusive breastfeeding and the impact of early breastfeeding cessation are underway to confirm this hypothesis.

- **Breastfeeding versus formula feeding.** A study conducted in Nairobi, Kenya (Nduati et al, 2000b), randomized 425 pregnant women to one of two groups, one using infant formula at birth (no breastfeeding), the other breastfeeding. Investigators measured MTCT rates, HIV-free survival, and mortality at 24 months of age. Mothers in the formula group were instructed on how to prepare the infant formula, including boiling water and cup-feeding on demand. Women in the breastfeeding group were instructed to breastfeed exclusively for 4 to 6 months, on demand, in accordance with Ministry of Health feeding recommendations. Data analysis was based on 401 live-born infants (197 were in the breastfeeding and 204 in the formula feeding groups). Of these infants, 17 percent were lost to follow-up before HIV status could be determined, and 7 percent were lost before mortality data could be ascertained. Compliance with the randomized feeding regimens was problematic. In the breastfed group, there was 96 percent compliance with "any breastfeeding" but mixed breastfeeding in early infancy was common. In the formula-fed group, only 70 percent of women completely avoided breastfeeding, suggesting the difficulty of implementing this type of intervention. The risk of HIV-transmission, calculated at 24 months, among breastfed infants was 36.7

percent compared to 20.5 percent for the formula fed group ($p<0.002$). Although overall mortality was not significantly different among the formula fed (20.0%) and breastfed infants (24.4%) at 24 months, HIV-free survival was significantly greater in the formula fed group (70 versus 58%). The researchers pointed out that the risk of postnatal transmission was not linear: 63 percent of postnatal infections occurred by six weeks; 75 percent by 6 months; and 87 percent by 12 months of age. Further analyses suggest that the risk of HIV transmission through breastfeeding also depends on the amount of breastmilk consumed by the infant (Richardson et al, 2000).

- **Duration of breastfeeding.** A study conducted in Malawi (Miotti et al, 1999) also observed that the risk of postnatal transmission through breastfeeding declined with infant age. In this study 672 infants born to HIV-positive mothers but uninfected at birth were followed to measure possible transmission by breastfeeding. The incidence of new HIV infections was 0.7 percent per month from months 1 to 5; 0.6 percent from months 6 and 11; and 0.3 percent from months 12 to 17. It is

RESEARCH PROFILE: ZAMBIA

HIV and Infant Feeding Options

A qualitative research study was undertaken in Ndola-Urban District to learn from communities and health providers about infant feeding practices; knowledge of mother-to-child transmission; attitudes toward HIV testing; and the safety of the UN-recommended replacement feeding options. The study was carried out in order to make recommendations for the introduction of an MTCT program, including recommendations about infant feeding options for HIV-positive women.

The research revealed that infant feeding options are very limited in the area because of economic and social concerns. Replacement feeding (with infant formula or modified cows' milk) costs about US$105 for the first 6 months. Women who do not breastfeed may be stigmatized as promiscuous and/or having HIV. In addition there are many misperceptions among health providers and families about MTCT, including transmission through breastfeeding.

Based on the research findings the MTCT project will promote breastfeeding for HIV-negative women and women of unknown status. All HIV+ women in the program will receive counseling about infant feeding options. HIV+ women who choose to breastfeed will be counseled to breastfeed exclusively for about 6 months. If they experience breast problems (cracked nipples, abscesses, or mastitis), they will be advised to continue breastfeeding with the unaffected breast while expressing and discarding milk from the infected breast. If they experience symptoms of fever, cough, diarrhea, or malaria, they will be advised to go to the health center right away.

Mothers who choose not to breastfeed, or to wean early, will be advised to cup-feed with infant formula, although diluted cows' milk (with additional sugar) may be used when formula is not available. Mothers will be advised to feed their babies 6 months and older with an enriched maize porridge prepared with milk, oil, and sugar at least 3 times/day. Specific recommendations for other foods and snacks, and hygiene-related practices were also developed based on locally-available resources.

The research highlighted that fact that several interventions are required to reduce MTCT of HIV, including primary prevention and income-generating activities to improve household food security, among others. Infant feeding counseling and other support must be available continuously because feeding decisions and individual and household circumstances change over time. Partner testing and male involvement should be encouraged in all MTCT programs.

Source: Piwoz EG, Chintu M, Ntombela N et al (1999).

not clear why breastfeeding-related transmission declines with age in this and in the Kenyan study. It is possible that there are specific infant or maternal characteristics, such as infant susceptibility (e.g., immature gut or immune system) or maternal infectivity, that modify breastfeeding risks with infant age. It is also possible that the amount of virus consumed declines with infant age, thus decreasing the risk of HIV transmission (Richardson et al, 2000).

- **Mastitis.** Mastitis is a local inflammation of the breast that causes tenderness, redness and heat (see Box, "Research Profile: Tanzania—Vitamin E and Mastitis"). Mastitis affects up to one-third of breastfeeding women, usually during the first 2 months after delivery. Mastitis has recently emerged as a possible risk factor for HIV transmission through breastfeeding. In a study in Blantyre, Malawi (Semba et al, 1999a), 334 HIV-positive and 96 HIV-negative women were followed from pregnancy to 12 months post-delivery. At 6 weeks post-partum, breastmilk samples were obtained and examined for elevated sodium concentrations, indicative of breast infection or inflammation. Researchers found that HIV infection itself was not a risk factor for mastitis, as 16.4 percent of HIV-infected women and 15.6 percent of uninfected women had elevated breastmilk sodium concentrations. Women with elevated breastmilk sodium levels had higher concentrations of immunologic factors (e.g., lysozyme, SLPI) in their breastmilk and lower concentrations of carotenoids in their blood than women without high milk sodium levels (Semba et al, 1999b). HIV-infected women with mastitis, however, had higher plasma HIV levels; lower CD4 cell counts; higher HIV viral loads detected in their breastmilk; and increased rates of MTCT at 6 weeks (45.4%) and 12 months of age (50.9%) than infected women without mastitis. After adjusting for maternal viral load and breastmilk HIV, women with mastitis at 6 weeks were 2.3 times more likely to have HIV-infected infants at 12 months than women without mastitis inflammation. Causes of mastitis and other clinical indicators of mastitis were not assessed. As noted in Chapter III.D.2., mastitis may be associated with maternal nutritional status. This study suggests that treatment of mastitis, which has relatively low morbidity and can be treated at low cost with antibiotics, may reduce HIV transmission through breastfeeding. The findings further confirm the importance of counseling women about proper breastfeeding and lactation management to avoid breast and nipple problems that may result in mastitis and increase transmission risk.

- **Colostrum.** The role of colostrum in breastfeeding-related HIV transmission is not well understood nor easy to study because it is not possible to distinguish between HIV infection acquired during late pregnancy or delivery and HIV infection acquired during the first days of life through breastfeeding. There are arguments for and against the theory that consumption of colostrum in the first days of life is more likely to result in HIV transmission than consumption of mature breastmilk. Arguments *for* increased risk include the high inflammatory cell counts in colostrum; the immature intestinal and immune system in neonates; and possibly also the higher viral concentration in colostrum, although this has not yet been demonstrated. Arguments *against* excess risk are evidence of a low proportion of infected cells in colostrum; the low volume of colostrum ingested, and higher concentrations of IgA and IgM (antibodies) as well as other anti-infective cells in colostrum that can offer protection against infection (Van de Perre, 1999).

Research must continue to provide a better understanding of the conditions associated with increased and reduced risks of HIV transmission through breastfeeding; the risks associated with alternative feeding practices; and the inputs and support that programs must provide to HIV-infected women who are faced with difficult decisions about how to feed their babies safely.

C. Antiretroviral Drug Trials for Prevention of MTCT

Short-course, prophylactic antiretroviral drugs (ARV) are the most effective way to reduce MTCT during pregnancy, labor and delivery, and through breastfeeding during the first days of infant life. The first short-course ARV protocols, using the drug zidovudine (ZDV), were tested in the United States and France. This protocol (known as AIDS Clinical Trials Group [ACTG] 076) required early identification of HIV-infection in pregnant women;

intravenous therapy during labor and delivery; no breastfeeding (to prevent postnatal transmission); and a very high budget, making the protocol only affordable in industrialized countries with sufficient resources. This protocol reduced MTCT in its study subjects by about two-thirds. This protocol was followed by a simpler, less costly regimen (see Box, "Research Profile: Thailand—Short-course AZT to Reduce MTCT") tested in Thailand, which reduced MTCT by about 50 percent, again among women who did not breastfeed (Shafffer et al, 1999).

Although less expensive than ACTG 076, the Thai regimen was also considered to be too expensive and complicated for widespread use in Africa, particularly among populations where breastmilk substitutes and related supplies were unavailable, unaffordable, and difficult to use safely. Many infant feeding experts also worried that promotion of infant formula and other breastmilk substitutes to women who received prophylactic ZDV in Africa could have a spillover effect – that is, women who did not know their HIV status or who were HIV-negative might begin to use infant formula, practice mixed feeding, or stop breastfeeding early because of fear of HIV. Switching unnecessarily from breastfeeding to artificial or mixed feeding, it was feared, could lead to increases in child morbidity and mortality.

These concerns have been somewhat alleviated by several clinical trials undertaken in Africa in the past few years to assess the efficacy of different short-course ARV protocols in breastfeeding women. The findings from these trials, available to date, are summarized below:

- **The DITRAME Trials.** These studies were carried out in Abidjan, Cote d'Ivoire, and Bobo-Dioulasso, Burkina Faso, where about 14 and 7.5 percent of pregnant women were HIV-positive, respectively. Women were randomly assigned to receive 300 mg of zidovudine (ZDV) twice daily from 36-38 weeks gestation, 600 mg at the beginning of labor, and 300 mg twice daily for 1 week post-partum (n=214) or a matching placebo (n=217). At 6 months, HIV transmission in the ZDV group was 18 percent, compared to 27.5 percent in the placebo group, with a relative efficacy of 38 percent ($p< 0.03$) (Dabis et al, 1999a). Follow-up to 15 months showed continued differences of 21.5 percent in the ZDV group versus 30 percent in the placebo group (Dabis et al, 1999b), for a relative efficacy of about 30 percent. Nearly half (43 percent) of study infants were still being breastfed at 15 months.

- **CDC/Abidjan Trial.** Another randomized, controlled trial was carried out in Abidjan which provided HIV-infected pregnant women with either a placebo (n=140) or ZDV (300 mg twice daily beginning at 36 weeks gestation, 300 mg at the onset of labor and every 3 hours until delivery; n=140) (Wiktor et al, 1999). This was

RESEARCH PROFILE: THAILAND

Short-course ZDV to Reduce MTCT

Clinical trials in the USA and France found that zidovudine (also known as ZDV or AZT) given orally five times per day to HIV-infected pregnant women beginning at 13-34 weeks gestation; intravenously during labor; and orally to non-breastfed babies for six weeks reduced MTCT by two-thirds (Connor et al, 1994). Although this regimen, known as 076, became the standard of care in the USA, it was too complex and costly for use in the developing world. Clinical researchers in Thailand, with support from the US Centers for Disease Control (CDC), conducted a randomized, placebo-controlled trial to assess the efficacy of a shorter course of AZT treatment for reducing MTCT. Mothers received 300mg of zidovudine two times per day beginning at 36 weeks gestation and every three hours from the start of labor until delivery. Mothers were given infant formula and asked not to breastfeed. MTCT was reduced by about 50 percent. In the treatment group only 9.4 percent of infants were HIV-positive at two months, compared with 18.9 percent in the placebo group ($p < 0.006$). About 80 percent of the reduction was attributed to lower maternal viral concentrations during delivery. This regimen appears safe and effective for reducing MTCT in non-breastfeeding populations.

Source: Shaffer N, Chuachoowong R, Mock PA et al (1999).

the same regimen as in the Thailand study except that all mothers breastfed their babies. At 3 months of age, transmission rates were 15.7 and 24.9 percent in the ZDV and placebo groups respectively ($p<0.07$), with a relative efficacy of 37 percent. Babies in the ZDV group were significantly less likely to die in the first 4 months of life.

A recent analysis combined the results of the DITRAME and CDC/Abidjan trials and found that, by 24 months, MTCT among placebo infants (N=322) was 30.2 percent compared with 21.9 percent among the infants exposed to ZDV. The postnatal transmission rates (from 6 weeks to 24 months) were similar between the treatment and placebo arms of the trials (about 9 percent). The researchers concluded that short-course, prophylactic ZDV remains effective at reducing MTCT in breastfeeding populations (Wiktor et al, 2000).

- **The PETRA Study.** PETRA was a multi-center, randomized controlled trial carried out in Johannesburg and Durban, South Africa; Dar es Salaam, Tanzania; and Kampala, Uganda (Piot, 1999). The study aimed to determine the efficacy, tolerance, and effectiveness of three drug regimens that included ZDV and lamivudine (3TC) for preventing MTCT of HIV. The three regimens included: a) drug therapy during the pre- (beginning at 36 weeks), intra-, and postpartum period (one week to mother and baby); b) drug therapy during the intra- and postpartum period only; c) drug therapy during the intra-partum period only; and d) placebo at all three time periods. Results of the trial are still being analyzed but preliminary results suggest HIV transmission rates of 6.7, 9.6, 15.8, and 16.4 percent in the four groups, respectively, at 6 weeks of age. HIV-free survival rates by 18 months were similar between groups, at about 79, 75, 72, and 73 percent, respectively, for the three study arms, although there were significant differences in mortality and breastfeeding practices among the study sites (Gray, 2000).

- **HIVNET 012 protocol.** Finally, the most recently promising ARV drug trial was carried out in Kampala, Uganda, using a protocol known as HIVNET 012. In this trial, 626 HIV-infected pregnant women were randomly assigned to receive either nevirapine (NVP; 200 mg orally at the onset of labor and 2 mg/kg to babies within 72 hours of birth) or ZDV (600 mg orally at the onset of labor, 300 mg every three hours until delivery, 4 mg/kg orally twice per day to babies for one week). Nearly all babies (99 percent) initiated breastfeeding and 96 percent were still breastfeeding at 14 to 16 weeks of age. At 14 to16 weeks, 13.1 percent of infants in the NVP group were HIV-positive, compared to 25.1 percent in the ZDV group ($p < 0.0006$), for a relative efficacy of 47 percent (Guay et al, 1999). At 12 months, 15.7 percent of the NVP babies were HIV-infected compared with 24.1 percent of infants receiving ZDV (Owor et al, 2000). The NVP protocol is particularly promising because of its low cost (about $4 per treatment compared to about $60 for the other short course therapies described above), and because only a single dose is required for mother and baby (Marseille et al, 1999). Trials are currently underway in South Africa and Zimbabwe to examine the safety and efficacy of different postpartum regimens of NVP for infants to reduce the risk of transmission through breastfeeding.

In summary, the recent drug trials conducted in Africa are encouraging. They suggest that short-course ARVs can significantly reduce MTCT in Africa. Although the efficacy of these drugs is diminished with prolonged exposure to HIV-infected breastmilk, the impact of short-course ARVs on MTCT is not completely lost when breastfeeding is practiced. Further research is needed to find ways to reduce HIV transmission through breastfeeding.

It is important to mention that all ARV protocols still require identification of HIV-positive women through voluntary counseling and testing (VCT) services. VCT services must be expanded throughout Africa so that affordable and effective interventions to prevent MTCT can be made available through routine health services and not only as part of clinical trials.

D. Recommendations for Making Breastfeeding Safer in the Context of HIV

The current UN policy statement on HIV and infant feeding emphasizes a mother's right to information and support that will enable her to make fully informed decisions about infant feeding

and empower her to carry these decisions out (UNAIDS et al, 1997). Ensuring that women are empowered to make fully informed decisions requires that they know their HIV status. Women must be given complete information and understand the consequences, both positive and negative of various feeding options for themselves and their children. Providing suitable support to enable them to carry out their decisions involves additional intervention to ensure that they have the skills and the resources available to safely carry out whatever decision they reach, be it to use replacement feeding or to breastfeed.

Today, the vast majority of HIV-infected mothers in Africa are not aware of their HIV status. This is a very important fact to bear in mind since most of the options for reducing MTCT discussed in the previous sections only apply to the minority of women who know that they are HIV-infected. The UN HIV and infant feeding guidelines clearly state that breastfeeding should still be protected, promoted, and supported among women who are HIV-negative or do not know their HIV status (UNICEF et al, 1998b).

In light of these realities, the following recommendations are offered for reducing the risk of HIV transmission through breastfeeding, while promoting optimal breastfeeding and complementary feeding practices (LINKAGES, 1999):

- Breastfeeding should be initiated immediately or within 30 minutes of birth.

- Health providers should ensure that good breastfeeding skills, including proper infant positioning and attachment, are established immediately.

- Infants should be breastfed frequently, day and night, and on demand, not according to a fixed feeding schedule.

- Infants should breastfeed exclusively for about 6 months (with no other liquids, milks, or solid foods introduced).

- Age-appropriate complementary foods should be introduced at about 6 months (unless growth faltering is observed in the presence of optimal breastfeeding between 4 and 6 months).

- Women who are at risk of HIV should take steps to prevent becoming infected during the breastfeeding period because the risk (rate) of transmitting the virus through breastfeeding roughly doubles (from about 15 to about 29 percent) during the period immediately following HIV infection (Dunn et al, 1992).

- Because recent studies also suggest that breast inflammation, cracked nipples, and other nipple or infant mouth sores increase the likelihood that the virus will be passed on through breastfeeding, women who are at risk of HIV should also seek immediate attention for all of these problems.

- Since many of these problems occur unilaterally (in one breast only), these women should also consider expressing and discarding breastmilk from infected breasts until such treatment is received.

Following these "safer" breastfeeding practices may help to reduce the risks of breastfeeding transmission of HIV among mothers who do not know their HIV status, among those who are HIV-negative but at high risk of becoming infected, and among women who are HIV-positive but have decided to breastfeed. When HIV status is unknown, pregnant women and their partners should be encouraged to learn their HIV status in order to able to make informed decisions about their own health and nutrition care and support, as well as the care and feeding of their children. At present, there is limited experience with counseling to fully inform and support women about HIV and infant feeding. Studies are underway in some countries to assess the impact of infant feeding counseling in the context of HIV on mothers' feeding decisions and infant outcomes. One study, conducted in Zimbabwe, found that even after being provided with full information, nearly all HIV-positive mothers still chose to breastfeed for cultural, economic, or personal reasons (Tavengwa et al, 2000). (See Box, "Research Profile: Zimbabwe—Impact of Infant Feeding Counseling in the Context of HIV").

In light of this, the concept of safer breastfeeding, although not presently one of the recommendations in the UN HIV and infant feeding guidelines, should be considered as one option for HIV-infected women who choose to breastfeed. A complete

description of safer breastfeeding practices is found in **Table 6**. Readers interested in a complete description of the other replacement feeding options are referred to UNICEF et al (1998b).

The impact of safer breastfeeding on postnatal transmission of HIV, infant morbidity, and mortality requires documentation. However, it is clear that successful safer breastfeeding has several prerequisites. First, it requires that mothers initiate breastfeeding immediately after birth and are able to establish good breastfeeding skills. This means that lactation support must be provided to women before birth and during the early postpartum period. Assistance for women who encounter problems should be available. Second, women must be willing and able to practice exclusive breastfeeding.

Successful program models to promote exclusive breastfeeding, though relatively common for urban populations in Latin America and Asia, have rarely been documented in Africa (Green, 1999). Recent studies of breastfeeding patterns in 69 developing countries showed that half of them have exclusive breastfeeding rates below 25 percent in infants under 4 months of age (UNICEF, 1997). Most studies in Africa reveal that the practice of exclusive breastfeeding is quite rare (e.g., Haggerty and Rutstein, 1999; Kuhn et al, 1999; Mukuria, 1999; Chopra et al, 2000; Gavin et al, 1999). Water, soft porridge, milk formula, or other foods are introduced early, often by the second month of life. The need to supplement breastmilk is often advocated by family members, neighbors, and health providers who are not aware of the benefits of exclusive breastfeeding and who doubt that breastmilk alone can nourish a baby. Therefore, any effort to promote exclusive breastfeeding will require the support of families, health providers, and community members.

RESEARCH PROFILES: ZIMBABWE

Impact of Infant Feeding Counseling in the Context of HIV

A study is underway in Harare to assess the impact of counseling about infant feeding in the context of HIV on mothers' decisions and practices. The study includes HIV testing of mothers at delivery, with pre-test and post-test counseling, including counseling on infant feeding. HIV-positive mothers are counseled on these options: 1) "safer breastfeeding," which includes exclusive breastfeeding, proper breast attachment/positioning, seeking medical attention for breast problems, and safe sex; 2) commercial and home-prepared infant formula; 3) expressing and heat-treating breastmilk; and 4) early cessation of breastfeeding. All other women are counseled on safer breastfeeding practices. Antenatal HIV-prevalence in this population is about 32 percent. Less than 10 percent of mothers chose to learn their HIV status in the first 2 months after delivery. Nearly all HIV-positive mothers who were counseled about replacement feeding options still chose to breastfeed (breastmilk substitutes were not provided by the study). To learn whether mothers were able to successfully practice "safer breastfeeding" after counseling, a subsample of 224 mothers of babies less than 2 months old were visited at home to assess information retention and practices. Of these, 70 percent were practicing exclusive breastfeeding (compared with 19 percent in the 1994 DHS for infants less than 2 months); 9 percent reported breast health problems (sore nipples, hot/redness, pain during feeding, engorgement); 57 percent demonstrated proper infant positioning and 27 percent proper attachment during breastfeeding; and 60 percent mentioned practicing safe sex as a way to reduce breastfeeding transmission. The researchers concluded that even with free testing and counseling, most women in this study area do not want to learn their HIV status, and after being fully informed, nearly all HIV-positive women breastfeed their babies. Safer breastfeeding practices are feasible, but they require cooperation and support from spouses, partners, and other family members.

Source: Tavengwa N, Ali F, Piwoz EG et al (2000).

TABLE 6. "Safer Breastfeeding" Practices for Women Infected or at Risk of HIV

All women who choose to breastfeed should …	HIV+ women who choose to breastfeed should also…
• Initiate breastfeeding immediately after birth. • Receive counseling and support to demonstrate appropriate infant positioning and breast attachment. • Receive counseling and support to encourage, understand, and implement the practice of exclusive breastfeeding. • Become familiar with the process of lactation in order to be able to identify potential problems associated with breastfeeding and how to overcome these while continuing to breastfeeding (e.g., breast engorgement, inflammation, sore nipples, etc.). They should know how to relieve engorgement with frequent emptying of the breast and hot compresses. • Receive counseling and support to encourage safe sexual activity and to understand the risk of HIV transmission through breastfeeding (and alternatives). • Receive counseling and support to continue breastfeeding and to introduce safe and appropriate complementary foods after 6 months.	• Be advised to express and discard breastmilk if there are signs of engorgement, blocked ducts, or inflammation. They should continue to feed from the unaffected breast. Medical attention should be sought if the engorgement or blocked ducts do not resolve within 1-2 days or if breast pain, fever, or other indication of mastitis or HIV disease progression is experienced. • Receive counseling and support describing the risks and benefits of early cessation of breastfeeding. On an individual basis, their ability to secure safe and appropriate replacement feeding should be assessed. They should be advised that continuing to breastfeed may still expose their baby to HIV but that early cessation of breastfeeding may increase the risk of poor growth and non-HIV diseases such as diarrhea. • Women who choose to discontinue breastfeeding should receive counseling and support to facilitate a rapid transition to replacement feeding.

In addition to the challenges posed by changing perceptions about exclusive breastfeeding, there is very little experience with programs to support and assist mothers with *other* elements of safer breastfeeding, such as early cessation of breastfeeding and seeking immediate medical attention for breastfeeding problems. Most breastfeeding promotion programs encourage mothers to breastfeed for 2 years or longer, and the recommendation to stop breastfeeding early will be completely new to most health workers and communities. Programs that promote early breastfeeding cessation must identify appropriate strategies for supporting mothers with this practice. This is necessary to reduce the risk of malnutrition and distress in babies who are abruptly weaned from their major source of nourishment and comfort. Women who seek frequent medical attention, on the other hand, may be suspected of being HIV-infected. Proper lactation management, treatment, and support services must be available to help women seeking care.

VI. Recommendations for Future Research

Further research is urgently needed on the nutritional management of HIV/AIDS in the African context, where HIV is spreading rapidly, where malnutrition is endemic, and where resources for management of both HIV and malnutrition are extremely constrained. Priorities are summarized below.

Nutritional management of HIV/AIDS

- Consensus must be reached on the recommended nutrient intakes for people with HIV, taking into consideration the changing nutritional requirements during the various stages of HIV infection and AIDS; the challenge of reversing metabolically-induced causes of weight loss; and the likelihood of nutritional deficiencies in the absence of HIV infection among adults and children in Africa and other developing countries.

- Research is needed to develop and test algorithms for the nutritional management of adults and children with HIV and AIDS in Africa. The effectiveness of different approaches (e.g., counseling, food supplementation, micronutrient supplements) for protecting the growth of children and/or for preventing weight loss among HIV-positive individuals who are not yet experiencing metabolic inefficiencies associated with the disease should be assessed.

- Setting-specific research is needed to identify foods and recipes that are appealing and appropriate, and that can protect the health and nutritional well-being of people with HIV and with AIDS. This would include recommendations for the best "nutritional buy" in a given area, given the physiologic and economic constraints faced by most people affected by HIV/AIDS.

- The impact of breastfeeding on the health and disease progression of HIV-infected women should be studied further.

- Studies are needed to determine the efficacy and safety of multiple micronutrient supplements for improving nutritional status, preventing HIV disease progression, and delaying AIDS-related mortality in populations that are endemically deficient and may also experience chronic food insecurity.

- The relative costs and benefits of alternative nutrition interventions for prolonging survival and improving the quality of life of PLWHA in Africa should be documented.

Reducing the risk of mother-to-child transmission

- Research is needed to document the impact of "safer breastfeeding" practices on postnatal HIV transmission, infant morbidity, and mortality. Additional risk factors for breastfeeding-related HIV transmission should be identified.

- Research is needed on the impact and effectiveness of MTCT programs that provide infant feeding counseling and education on infant feeding decisions, practices, and biological outcomes. The health-related outcomes (MTCT, morbidity, mortality) associated with different infant feeding patterns (e.g., exclusive breastfeeding, early breastfeeding cessation) and breastfeeding conditions should be determined.

- Research on the safety and efficacy of affordable antiretroviral drugs to reduce HIV transmission during breastfeeding is also needed.

- The impact of nutritional interventions during pregnancy and post-delivery on maternal health status, HIV transmission through breastfeeding, and infant health and survival should be studied.

- Feasible protocols for assessing breast health and treating conditions that are associated with increased HIV transmission through

breastfeeding (e.g., mastitis, cracked nipples, breast sores, infant mouth sores) are required. Since increased HIV transmission may be associated with sub-clinical breast inflammation, such protocols should be designed so mothers can use them to monitor their own breast health and control the safety of their breastfeeding practices.

- Continued research is needed to identify the timing of HIV transmission, particularly transmission occurring during labor and delivery versus the first weeks of infancy. Improvements in HIV diagnostic technology are also needed to facilitate the understanding of the role of colostrum in HIV transmission, as well as the understanding of other risk factors associated with breastfeeding transmission in early infancy.

- Setting-specific studies are needed to identify the affordability, acceptability, and safety of various alternative infant feeding options, as well as the psychological, social, economic, and other consequences of replacement feeding on women and their children.

- Countries should actively monitor infant feeding trends and compliance with the International Code for Marketing of Breast Milk Substitutes (BMS) to assess the impact of MTCT programs on breastfeeding practices in the general population and to minimize the adverse consequences of information on replacement feeding for HIV-infected women and BMS marketing in the general population.

- The relative costs and benefits of alternative interventions reducing postnatal transmission of HIV in Africa should be documented.

Human and financial resources are needed to implement the research and program recommendations described in this paper. Without such resources, it will not be possible for African countries to provide adequate nutrition care and support for their citizens. The quality of life and the odds of survival for millions of African adults and children living with HIV and AIDS today, and those who are likely to be infected in the future, will remain bleak.

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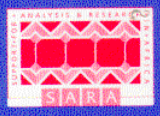

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