NUTRITION AND HIV/AIDS

Nutritional Guidelines for HIV-infected Adults and Children in Southern Africa: Meeting the Needs

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'Despite progress in boosting democracy, ending wars and improved economic growth, Africa is the only region in the world becoming less able to feed itself'.[1]

1. NUTRITION, WEIGHT LOSS AND HIV IN AFRICA

1.1 INTRODUCTION

The HIV epidemic affects large numbers of people living in the southern African region.[2] Despite more than 2 decades of research, a cure remains elusive.[3] The implementation of proven preventive interventions has had limited success; and the uptake of antiretroviral (ARV) drugs has lagged far behind the estimated numbers in need.[4] Furthermore, the production of food in Africa may well be adversely influenced both by the epidemic itself and by global warming.[5] Nutrition, specifically the use of food, special diets, micronutrients and so-called immune boosters and supplements, has been suggested as an affordable and practical means of 'delaying the onset of advanced HIV infection'.[6] Is this true? And if it is, how secure is access to food and good nutrition in Africa? Floods, drought, famine, poverty, war and political instability define much of the everyday life of millions on this continent. Secure and reliable access to food is extremely important in these circumstances. In some instances, sex will be exchanged for food and employment far from home may result in risky sexual behaviour. The science of nutrition is more than the science of food itself.[5] It is about people, their access to food of a suitable quality and quantity, and in addition it is about the production of food and its utilisation. It is also about maintaining access to food over decades so as to ensure that the children and adults of Africa – including those who are HIV-infected – grow and realise their full potential.

Discussion about food and diet in the HIV era also requires that due attention be given to the interactions and toxicities of the ARV group of drugs. These have revolutionised the management of HIV infection. Sooner or later all who are infected will need to take these agents. Some ARVs are best given on an empty stomach, some with food and others with a fatty meal. Many give rise to metabolic alterations, such as insulin resistance and glucose intolerance, fat abnormalities (lipodystrophy, hyperlipidaemia), lactic acidosis, liver enzyme abnormalities, anaemia and osteopenia.[7] Certain herbs and foods interfere with the bioavailability of the ARVs. Various micronutrients have been shown to benefit the HIV-infected. Home-grown diets, herbal concoctions and vitamin supplements have been advanced by some as alternatives to the ARVs and as cures of the disease, but without providing evidence of their benefit.[8] Where denial and stigma and commercial interests have dictated the political and social response to this epidemic, it has been a simple matter to add nutritional nonsense and personal economic gain to the general confusion that has defined public discussion.[9]

The science of nutrition and HIV infection intersect at several strategic levels. Evidenced-based research confirms the following four concepts:

- Weight loss predicts death.[10]
- Energy and nutrient needs are increased in the HIV-infected.[11]
- Adequate food – and not just vitamins and so-called immune boosters – constitutes an appropriate supplement for those in need.[12]
- Nutritional security: Food alone is not enough. Children and adults who are malnourished, whether they are infected, exposed or affected, need comprehensive medical and nutritional care and social support.[13]

These concepts will be discussed in detail in later chapters.

1.2 EPIDEMIOLOGY AND BASIC SCIENCE

The human immunodeficiency virus (HIV) crossed into the human race from its primate host in the early decades of the 20th century.[14] Since that time it has spread throughout the globe and has caused more than 20 million deaths worldwide.[15] Sub-Saharan Africa has borne the greatest burden of the infection. Without access to ARV drugs average

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survival is about 10.3 - 10.8 years.[16] The HIV virus is spread from human to human via direct contact with sexual fluids and blood (blood products) and to infants and children during pregnancy and lactation.[17] Since the mid-1990s, drugs called antiretrovirals (ARVs) have been used to control viral replication, and to prevent neonatal transmission and accidental exposure to the virus. These interfere with the growth cycle of the virus. Some prevent the virus from entering the human cell (viral entry inhibitors), while others inhibit viral enzymes that assist in the reproduction of the virus: the nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs and NtRTIs) and the non-nucleoside reverse transcriptase inhibitors (NNRTIs). The protease inhibitors (PIs) block the assembly of newly formed viral proteins. A further class of ARVs, the integrase inhibitors, impair the integration of viral DNA into the human genome. Interactions with food and other drugs, including herbs and the so-called immune boosters, are well documented. These interactions may impair viral control by a variety of mechanisms.

The virus targets the cells of the immune system, particularly the CD4 lymphocyte (the 'helper-T cells').[18] Despite the increased production of these cells, they are ultimately sacrificed to the virus. Eventually this progressive immune deficiency leads to life-threatening infections and cancers: the acquired immunodeficiency syndrome (AIDS). Once within a cell, HIV-1 reproduces rapidly. From a single infected cell thousands of new viral particles are released into the bloodstream. In the laboratory this is measured as the viral load. Nevertheless, most of the virus remains undetectable within the cells of the body.[19] Together with the medical history and examination, the measurement of the CD4 cell count and the viral load (VL) provide a platform from which to assess the patient. Because of the effect of the infection on nutritional status, this assessment should include the nutritional evaluation of the patient. What does growth failure and loss of weight mean in HIV-infected children and adults?

1.3 WEIGHT LOSS IN HIV-INFECTED CHILDREN AND ADULTS

Weight loss is a strong predictor of death in HIV-infected adults and children.[20]

WEIGHT LOSS PREDICTS DEATH

- Low weight reflects advancing disease
- Weight loss often indicates opportunistic infections or progressive disease
- Weight loss should be a warning to the doctor/nurse to initiate investigations and treatment

During the 1980s and early 1990s, 'Slim Disease' was a term used throughout central Africa to characterise a patient with end-stage HIV infection or AIDS.[21] Indeed, weight loss is used in both the World Health Organization (WHO) and the Centers for Disease Control (CDC) adult staging systems: unintentional weight loss of < 10% = WHO stage II and > 10% = stage III and CDC stage C, i.e. is AIDS defining.[22] In children older than a year, weight loss resulting in a fall of 2 or more percentile lines is AIDS defining if accompanied by chronic diarrhoea or fever. Also AIDS defining is a child in the 25th percentile of weight-for-height (on consecutive measurements separated by more than 30 days).[23] Severe wasting in adults is defined by the CDC as a body mass index (BMI) < 18.5 $(kg/m)^2$ or unintentional weight loss of > 5% of usual body weight within 6 months.[24] Growth faltering and stunting are common in children with HIV infection and occur early in life.[25-27] In children, wasting is particularly associated with the loss of lean body mass and failure to gain height.[27]

Weight = heaviness measured in kilograms

Lean body mass = the total of all body components except storage lipid (fat) and bone

Fat-free mass = the same as lean body mass

In adults both lean mass and fat are lost, though the loss of lean mass predominates.[24] In contrast, starvation leads primarily to fat loss.[24] Both the loss of lean mass and poor linear growth in HIV-infected children are closely associated with poor survival and protecting lean body mass prolongs survival.[24, 27]

Weight loss in the HIV-infected is the sum of a number of causes. Energy requirements are increased even in the asymptomatic state.[28,29] These needs soar under periods of stress and during malnutrition.[29] Cytokines such as tumour necrosis factor-α (TNF-α) and interleukin-1 (IL-1) released during episodes of infection and even during the 'asymptomatic' phase of HIV infection, promote increased metabolism, glucose recycling, muscle catabolism and negative nitrogen balance.[29,30] They may also reduce appetite even when there is no overt opportunistic disease. This results in the characteristic wasting associated with AIDS.[31] Levels of interferon-α (INF-α) are persistently elevated in full-blown AIDS.[29,31] Apart from these underlying metabolic factors, the inability to eat or to swallow food and the increased loss of dietary nutrients from vomiting and diarrhoea will lead to wasting and malnutrition. Wasting also accompanies the opportunistic infections and cancers of advanced HIV-infection.

1.4 WEIGHT LOSS: ITS CAUSES AND INCREASED ENERGY REQUIREMENTS (Table 1.1)

1.4.1 Increased and often unmet energy requirements during all stages of HIV infection

Energy requirements are likely to increase by 10% just to maintain body weight and normal physical activity in asymptomatic HIV-infected adults and to maintain normal growth in asymptomatic, infected children. During symptomatic stages and particularly during AIDS (opportunistic diseases) these energy requirements increase by 20 - 30%. Energy needs may even increase to levels of 50 - 100% above

TABLE 1.1. INCREASED ENERGY NEEDS OF HIV-INFECTED ADULTS, ADOLESCENTS AND CHILDREN[28,29]

	HIV-positive phase	Energy
Adults and adolescents	Asymptomatic	10%↑
	Symptomatic (mild)	20 - 30%↑
Children	Asymptomatic	10%↑
	Symptomatic (mild)	20 - 30%↑
	Symptomatic (moderate to severe)	50 - 100%↑*

*In the presence of severe malnutrition.

normal in children who are severely malnourished and who are experiencing weight loss.[28,29] When enriched with various fats (peanut butter) or oils (olive, canola), food will provide greater 'energy content'. This 'enriched' food is needed to supplement the daily, baseline dietary requirements if the malnutrition and weight loss are to be corrected.

MANAGING WEIGHT LOSS EFFECTIVELY

- Record weight at each visit, usually 3 - 4 visits annually.
- Identify the reason for the weight loss
- Control the HIV infection where indicated: ARVs may be needed
- Treat malnutrition: Food, supplements, micronutrients where needed
- Diagnose and treat opportunistic disease
- Symptomatic control of: Nausea, anorexia, vomiting, diarrhoea
- Examine the oral cavity: Treat thrush, gingivitis and oral ulcers
- Stop smoking, alcohol abuse and recreational drug use
- Exercise and strength training may have a role in some
- Exclude hypogonadism (rare) and consider use of appetite 'stimulants' such as megesterol acetate, anabolic steroids and dronabinol for nausea where appropriate (benefit controversial)
- Involve social support mechanisms: Social worker, income grants, NGOs including faith-based groups that provide nutritional support, exclude depression and anxiety, consider incorporating a family member or 'concerned other'.

1.4.2. Decreased energy intake and the increased loss of nutrients

Anorexia, nausea, gingivitis, oral sores and dysphagia will impair food intake and promote weight loss. At times the ARVs and the anti-TB drugs are poorly tolerated – nausea, anorexia, and vomiting. Fortunately this situation is generally short-lived and usually restricted to the first weeks after the start of therapy. Depression and anxiety suppress appetite and result in weight loss. Religious and cultural practices that require regular fasting, purging and dietary restrictions may be harmful in the context of advanced HIV infection. Food access and food security can be significantly affected when material resources are lost - income, the inability to work. Chronic diarrhoea and malabsorption may cause wasting: direct viral invasion of gastrointestinal cells (HIV-enteropathy) can be demonstrated in some patients.[32] Both localised gastro-intestinal and overwhelming generalised infections are frequent in Africa. Pulmonary and extra-pulmonary TB, salmonella, *Escherichia coli,* cryptosporidia and isosporiasis may present with fever, anorexia, nausea, vomiting and diarrhoea. Undiagnosed and untreated, these infections will lead to wasting and ultimately death.

The prevention and treatment of weight loss is a priority for patients who are HIV-infected. What can be done for patients who are at risk?

1.5 WEIGHT LOSS. ASSESSMENT AND TREATMENT

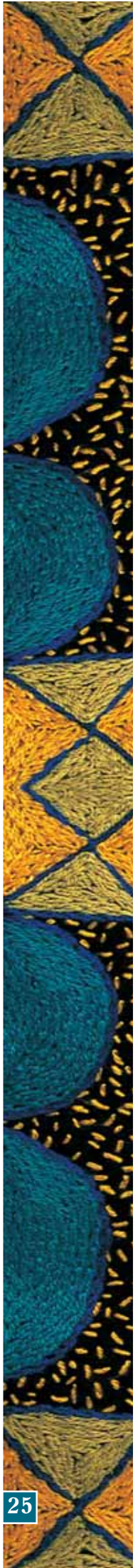
1.5.1 Assessing weight loss

All infected children and adults must be regularly followed up. This includes taking a medical and nutritional history. The patient must be thoroughly examined. It goes without saying that in southern Africa, every effort MUST BE MADE to identify the infected so as to offer them protection from advancing HIV disease and facilitate the control of the epidemic. The following measurements are essential: weight, height/length in children, the mid-upper arm circumference (MUAC) and the CD4 and viral load. MUAC is a useful means of assessing lean body mass. Additional investigations are discussed in a subsequent section.

1.5.2 Managing weight loss

Attention must be given to the causes of weight loss and the diagnosis and control of anorexia. Poverty, food insecurity and related socio-economic issues ought to be recognised and managed in as practical a way as possible. The timeous provision of ARV therapy is a very appropriate means of preventing weight loss and the secondary opportunistic infections associated with it.[33]

Provide food. Provide nutritional counselling. Provide support – but aim to make the patient and their family independent of food parcels and short-term solutions. A team approach (nurse, doctor, dietician and trained nutritional advisor) works best. Diagnose and treat intercurrent disease. Check the CD4 and viral load and any other relevant tests as suggested by the clinical examination. Consider starting ARV therapy where appropriate. 'The best way to achieve protein repletion in clinically severe HIV/AIDS is to establish effective ARV therapy.'[34] Once an adult has achieved his/her normal body weight, discourage further weight gain in those on ARVs. Obesity is to be avoided. Fat redistribution, hyperglycaemia and insulin resistance, the metabolic syndrome, hyper-lipidaemia and cardiovascular disease are recognised complications.[35-37] Wasting and severe malnutrition may require enteral and parenteral feeding. This is usually undertaken in a hospital or clinic. Nutritional supplements such as fortified porridges and food itself ought to be accessed on behalf of the patient. The use of specific micronutrients generally follows recommendations for the population at large. Safety, tolerability and cost are the important drivers in this regard.[24] The role of individual supplements will be discussed later. Exercise – including resistance training – has been found to improve the patient's quality of life, to build up lean body mass, and in those on



ARVs, to improve serum lipid profiles.[38,39] The simplest monitor of nutritional recovery in adults is the measure of sequential weight gain. But weight alone will not discriminate between the return of lean muscle and/or fat, or for that matter indicate the return of good health. Other measurements in addition to that of weight will be needed.

REFERENCES

1. Christian Science Monitor. Hunger is spreading in Africa. August 01, 2005. http://www.csmonitor.com/2005/0801/p01s02-woaf.html
2. Merson MH. The HIV-AIDS Pandemic at 25 – The Global Response. *N Engl J Med* 2006; 354: 2414-2417.
3. Hammer SM, Saag M, Schechter M, *et al*. Treatment for adult HIV infection: 2006 recommendations of the International AIDS Society-USA panel. *JAMA* 2006; 296: 827-843.
4. Hassan F, Bosch D. Monitoring the Provision of ARVs in South Africa: A Critical Assessment. Aids Law Project, University of the Witwatersrand. ALP Briefing for TAC, NEC on 17 and 18 January 2006, Cape Town.
5. de Waal A, Whiteside A. New variant famine: AIDS and food crisis in southern Africa. *Lancet* 2003; 362: 1234-1237.
6. Smetherham J-A. Mrs v d Maas and the AIDS diet. Cape Times. 2004; 27 February.
7. Montessori V, Press N, Harris M, Akagi L, Montaner JSG. Adverse effects of antiretroviral therapy for HIV infection. *CMAJ* 2004; 170: 229-238.
8. http://www4.dr-rath-foundation.org/THE_FOUNDATION/press_release 20050615.htm
9. Health Ministry backs AIDS muti. City Press report on News24.com, 13 February 2006. http://www.news24.com/News24/South_Africa/Aids_Focus/ 0,,2-7-659_1880449,00.html
10. Wheeler DA, Gilbert CL, Launer CA, *et al*. Weight loss as a predictor of survival and disease progression in HIV infection. *J Acquir Immune Defic Syndr* 1998; 18: 80-85.
11. Mangili A, Murman DH, Zampini AM, Wanke CA. Nutrition and HIV infection: Review of weight loss and wasting in the era of highly active antiretroviral therapy from the Nutrition for Healthy Living Cohort. *Clin Infect Dis* 2006; 42: 836-842.
12. Young H, Borrel A, Holland D, Salama P. Public nutrition in complex emergencies. *Lancet* 2004; 365: 1899-1909.
13. Finch L. Fighting for food aid – the struggle to assist groups affected by HIV/AIDS. *Lancet* 2004; 364: 1650-1651.
14. Stebbing J, Gazzard B, Douek DC. Where does HIV live? *N Engl J Med* 2004; 350: 1872-1880.
15. Sepkowitz K. AIDS – the first 20 years. *N Engl J Med* 2001; 344: 1764-1772.
16. The UNAIDS Reference Group on Estimates, Modelling and Projections. Improved methods and assumptions for the estimation of the HIV/AIDS epidemic and its impact: recommendation of the UNAIDS Reference Group on Estimates, Modelling and Projections. *AIDS* 2002; 16: W1-W14.
17. Schreibman T, Friedland G. Human immunodeficiency virus infection prevention: Strategies for clinicians. *Clin Infect Dis* 2003; 36: 1171-1176.
18. Rosenberg ES, Walker BD. HIV Type 1-specific helper t cells: a critical host defence. *AIDS Research Human Retrovir* 1998; 14 (Suppl 2): S143-S147.
19. Kilby JM. Human immunodeficiency virus pathogenesis: insights from studies of lymphoid cells and tissues. *Clin Infect Dis* 2001; 33: 873-884.
20. Tang AM, Forrester J, Spiegelman D, Knox TA, Tchetgen E, Garbach SL. Weight loss and survival in HIV-positive patients in the era of highly active antiretroviral therapy. *J Acquir Immune Defic Syndr* 2002; 31: 230-236.
21. Serwadda D, Mugerwa R, Sewankambo N. Slim disease: a new disease in Uganda and its associations with HTLV-III infection. *Lancet* 1985; 2: 849-852.
22. The WHO International Collaborating Group for the Study of the WHO Staging System. Proposed 'World Health Organisation Staging System for HIV Infection and Disease': preliminary testing by an international collaborative cross-sectional study. *AIDS* 1993; 2: 711-718.
23. Bailey RC, *et al*. Growth of children according to maternal and child HIV, immunological and disease characteristics: a prospective cohort study in Kinshasa, Democratic Republic of the Congo. *Int J Epidemiol* 1999; 28: 532-540.
24. Grinspoon S, Mulligan K. Weight loss and wasting in patients infected with human immunodeficiency virus. *Clin Infect Dis* 2003; 36 (Suppl 2): S69-78).
25. Bobat R, Coovadia H, Moodley D, Coutsoudis A, Gouws E. Growth in early childhood in a cohort of children born to HIV-1 infected women from Durban, South Africa. *Ann Trop Paediatr* 2001; 21; 203-210.
26. Miller TL *et al*. Growth and body composition in children infected with the human immunodeficiency syndrome virus-1. *Am J Clin Nutr* 1993; 57: 588-592.
27. Arpadi SM. Growth failure in HIV-infected children. WHO Consultation on Nutrition and HIV/AIDS in Africa: Evidence, lessons and recommendations for action. Durban, 10-13 April 2005. Geneva: World Health Organization, 2005.
28. Food and Nutrition Technical Assistance (FANTA) Project. *HIV/AIDS: A Guide for Nutritional Care and Support*. 2nd ed. Washington, DC: Academy for Educational Development, 2004: 86.
29. Hsu J W-C, Pencharz PB, Macallan D, Tomkins A. Macronutrients and HIV/AIDS: A review of current evidence. WHO Consultation on Nutrition and HIV/AIDS in Africa: Evidence, lessons and recommendations for action. Durban, 10-13 April 2005. Geneva: World Health Organization, 2005: 1, 2.
30. Roubenhoff R, Grinspoon S, Skolnik PR, *et al*. Role of cytokines and testosterone in regulating lean body mass and resting energy expenditure in HIV-infected men. *Am J Physiol Endocrinol Metab* 2002; 283: E138-145.
31. Hazenberg MD, Otto SA, van Benthem BHB, *et al*. Persistent immune activation in HIV-1 infection is associated with progression to AIDS. *AIDS* 2003; 17: 1881-1888.
32. Kotler DP. HIV infection and the gastrointestinal tract. *AIDS* 2005; 19: 107-117.
33. Gazzard B. Antiretroviral therapy for HIV: medical miracles do happen (Editorial). *Lancet* 2005; 366: 346-347.
34. Shevitz AH, Knox TA. Nutrition in the era of highly active antiretroviral therapy. *Clin Infect Dis* 2001; 32: 1769-1775.
35. Grunfeld C, Feingold KR. Metabolic disturbances and wasting in the acquired immunodeficiency syndrome. *N Engl J Med* 1992; 327: 329-337.
36. Dube MP. Disorders of glucose metabolism in patients infected with human immunodeficience: effects on parameters related to fatigue, dyspnea, weight and body composition in HIV-infected adults. *AIDS* 2001; 15: 693-701.
39. Roubenoff R, McDermott A, Weiss L, *et al*. Short-term progressive resistance training and lean body mass in adults infected with human immunodeficiency virus. *AIDS* 1999; 13: 231-239.

2. NUTRITION, HIV AND CLINICAL MEASUREMENT

2.1 NUTRITION: TAKING A DIETARY HISTORY

'A simple nutritional assessment is available to all and requires only an interview, a scale and a tape measure.'[1] This assessment begins with history taking: 'What do you eat on a typical day?' 'When last did you have a meal?' 'Tell me everything you've had to eat or drink in the last 24 hours.' The nutritional history needs to give the interviewer a clear sense of the client's diet, its contents, amounts of food taken, regular and reliable access to good food, and in the context of the HIV epidemic, the stage of the infection and use by the client of prescribed medication, herbs and traditional or so-called complementary treatments.

It may be helpful to use actual plates, cups and spoons to estimate the size of food portions. A diary card may be helpful: 'Record everything you eat and drink for the next week. Add in the amounts that you consume ...'[2] If the patient is an infant, enquire as to what feeds are being given. Formula? Breast? Exclusive or mixed breastfeeds? How is the food prepared? What understanding does the client have of hygiene and food? ARV drugs may cause physical changes: ask about weight loss and breast enlargement and the loss of fat on the face, arms and legs. What is the stage of HIV infection? Have opportunistic diseases such as TB been experienced? Co-morbid conditions such as diabetes, liver and cardiovascular disease will require dietary advice and the outlining of potential ARV drug and food interactions.[3,4] 'Do you or the family ever go without food?' Enquire about the patient's access to an income and food. In busy public clinics trained caregivers from the community can assist with history taking, and the weighing and measuring of patients. The goal of the dietary analysis is to prevent weight loss and optimise nutrition: the counselling that takes place will foster the patient-doctor/nurse relationship and improve communication.[5,6] However, providing specific advice is difficult. Diets vary between and within populations. Familiarity with local foods, food preparation and the culture and traditions of a

community will root any advice offered within the context of the patient's life. Dietary advice needs to be culture sensitive and feasible. See also Appendices 1 and 2 for action to be taken in response to nutritional risk.

DIET HISTORY

A diet history is a detailed dietary record that may include a 24-hour recall, a food frequency questionnaire and other information such as weight, history, previous dietary changes, the use of supplements and known food intolerance.

NUTRITIONAL QUESTIONNAIRE

Question 1. Baseline assessment. What is your usual weight and height (adult)? Is the child being regularly weighed and having his/her height/length measured at the clinic? May I see the child's clinic card, please?

Question 2. Weight loss: Have you recently lost weight? Do your clothes still fit? Have you noticed weight gain and body changes on the antiretrovirals (ARVs)?

Question 3. Appetite: Has your appetite changed?

Question 4. Digestion: Do you have any of the following:

- Difficulty with swallowing?
- Discomfort or pain in the mouth?
- Nausea and vomiting?
- Diarrhoea?

Question 5. Food access and food security: In the past week have you missed any meals? Do you or your children ever go hungry? Are you able to eat meat or fish regularly? How often?

Question 6. Non-prescription medication. Do you take any immune boosters, vitamin supplements or traditional medicines? How much alcohol and/or recreational drugs do you take each day or each week?

Question 7. Prescription medication. Do you know which of your ARVs need to be taken with or without food/a meal? What medicines other than ARVs are you taking?

Question 8. Stage of HIV infection: Have you been admitted to hospital or been diagnosed with tuberculosis in the last 3 to 5 years? Do you know your most recent CD4 level?

2.2 NUTRITION: MEASUREMENT

Medical science is built upon practices that have measurable and reproducible outcomes. The measurement of human nutrition is based upon anthropometric, biochemical, clinical and dietary parameters – the so-called 'ABCD' of nutritional assessment.[7,8] Included in the anthropometric measurement are body weight, length or height, the body mass index (BMI) and the mid-upper arm circumference (MUAC). If performed reliably, these form a baseline from which to judge growth failure or abnormality. Often the measurements can be carried out by a trained non-medical clinic or community member. Results must be tabulated in the clinic file at each visit, preferably before the patient is seen by the nurse or doctor. A reduction in lean body mass in children is detectable before a deceleration in linear growth (length/height) and is important to document and act upon.[9] Waist circumference is a measure of cardiovascular risk, type 2 diabetes, hypertension and increased cholesterol risk in non-HIV infected adults. This may also be a helpful measurement in patients on ARVs at risk for the metabolic complications of therapy.[10]

Paediatric growth charts record both height and weight: height-for-age, weight-for-age, and weight-for-height. All three measurements must be plotted at each visit.[8] In young children, body length will replace height. MUAC and subscapular and triceps skin-fold thickness reflect lean body mass and fat stores in adults and children older than 1 year. About 50% of body fat is subcutaneous.[11,12] MUAC is generally the preferred measurement. MUAC is an essential component of malnutrition assessment and is routinely used in World Health Organization (WHO) and UNICEF-sponsored relief programmes.[6] Intercurrent illness will alter these measurements: repeated measurement reveals the emergence of trends and the early onset of new disease.

MUAC IN ADULTS AND CHILDREN

By convention the tape is placed around the left upper arm midway between the tip of the acromion process (shoulder) and the olecranon (elbow). Values in adult men of < 23 cm and women of < 22 cm represent malnutrition. Paediatric measurements vary with age and will be detailed in the (later) paediatric chapter.

WEIGHING THE PATIENT

Subjects are weighed in light underclothing without shoes. Heavy items of jewellery, wallet, keys, etc. should be removed and the patient advised that a large meal just prior to the measurement and a full bladder at the time of measurement will increase the reading. Where available a beam or lever balance is more reliable. Bathroom scales are generally unreliable. The scale must be regularly serviced and checked, preferably monthly. Babies are weighed naked and without their nappies.

In adults the body mass index, BMI = weight (kg)/height $(m)^2$ (Table 2.1), is a sensitive measure of both under and over nutrition. (The BMI can be read directly from a nomogram – usually present in most practices, or worked out from the above equation.)

TABLE 2.1. THE BODY MASS INDEX (BMI) – A MEASURE OF THE RISK OF UNDERNUTRITION AND OBESITY

Classification	BMI (kg/m^2)
Severe undernutrition	< 16
Underweight	< 18.5
Normal	18.5 - 24.9
Overweight	25.0 - 29.9
Obesity, class I	30.0 - 34.9
Obesity, class II	35.0 - 39.9
Extreme obesity, class III	> 40

Source: National Heart, Lung and Blood Institute, National Institutes of Health, USA. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. NIH Publication No. 98-4083.

2.3 NUTRITION: THE LABORATORY

Laboratory tests in HIV patients are restricted to those with clinical value. The CD4 cell count and viral load are essential and provide a direct measure of the patient's immune system and the virus. Often included in the routine workup are tests that indicate whether vital organs are functioning normally: blood, the full blood count (FBC); liver – the alanine aminotransaminase (ALT) level; and kidneys – urea or creatinine and urine dipstix. From time to time sophisticated diagnostic tests are indicated (blood cultures, malaria smears, sputum analysis for TB and urine microscopy), but tests that directly measure the micronutrient status of the patient are seldom required. In general, the clinical evaluation and anthropometric measurements discussed above will guide the clinician in deciding what additional investigations are necessary.

2.3.1 Anaemia

Anaemia is an independent predictor of mortality in HIV patients. It is therefore important to document and to follow and act upon.[13] The common nutritional deficiencies associated with anaemia are iron, folate and vitamin B_{12}. However the most common cause of anaemia in HIV-infected patients is 'the anaemia of chronic disorders', an anaemia seen in many chronic inflammatory or infective conditions and not related to any nutritional deficiency.[14] The haemoglobin, red cell mass and haematocrit are decreased. The laboratory will provide a comment on the peripheral blood smear and record the mean corpuscular volume (MCV), a measure of the size of the red cell. The MCV is usually normal in the anaemia of chronic disorders (normocytic anaemia), while in iron deficiency the red cells are small and the MCV is less than normal (microcytic anaemia). In folate and B_{12} deficiencies, the MCV will usually be elevated (macrocytic anaemia). Other causes of anaemia are occasionally present: red cell haemolysis, drug-induced toxicity (the ARVs: zidovudine, combivir), bone marrow infiltrate (e.g. tumour or infection such as TB) or infection with HIV itself. Not every HIV-infected person requires iron supplementation. Indeed most have an excess of storage iron (ferritin), and added iron may be harmful.[15,16] Nevertheless during pregnancy and lactation supplementation with iron, folate and multivitamins is given to both HIV-infected and non-infected women. In other circumstances, iron supplementation should only be provided if iron deficiency has been confirmed on laboratory testing. In many parts of Africa malaria and hookworm infestation are common. These must be excluded in any investigation of anaemia in patients from rural or endemic areas.[17]

2.3.2 Serum micronutrients in the HIV-infected patient

The persistent presence of the virus in the human host ensures that the immune system is chronically stimulated. Hence the frequently elevated total proteins in HIV-positive patients – resulting from the chronic overproduction of gamma globulins, including antibodies. Intercurrent illnesses cause additional inflammatory stress. An 'acute-phase response' follows. For the clinician, elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level help to define such periods.[18,19] Local and systemic cytokine levels rise and fall. Micronutrient concentrations mirror these changes. Some increase, others decrease.[20,21] Some micronutrients such as vitamins A, C and E, and zinc may behave as antioxidants. Low serum levels may therefore indicate utilisation rather than an underlying deficiency.[22,23] Blood levels are an incomplete measurement of the body's micronutrient status. Without the clinical context of the patient and knowledge of the micronutrient status of the community, the meaning of an individual result is of limited value.[24] Studies from the Cape and KwaZulu-Natal confirm generally low levels of micronutrients among HIV-infected South African children and adults.[25-27] Furthermore, micronutrient supplementation with vitamin A reduces morbidity, growth failure and death, while zinc supplementation reduces the duration of diarrhoea and associated fluid losses in young HIV-positive children.[27,28] Selenium and zinc also behave as acute-phase reactants: their levels fluctuate during infection. The value of observational and cross-sectional micronutrient studies and studies that ignore the acute-phase phenomenon remain difficult to interpret.[29-31] Any measurement of individual micronutrients must place the result within its clinical context. Where these issues are ignored, clinical studies fail to provide convincing data.[29] The routine measurement of micronutrients is expensive, difficult to interpret and generally not warranted in the southern African situation. But it goes without saying that well-planned clinical studies in this area are urgently needed to supplement the sparse data currently available.

2.3.3 Liver function tests: albumin and serum ALT

A low serum albumin level may indicate poor nutrition, and indeed low serum albumin predicts both death and length of stay in hospitalised HIV-positive patients.[5] But malnutrition is just one of several causes of low albumin: liver disease with decreased protein synthesis, renal disease with protein loss (albuminuria), enteric infections with chronic diarrhoea and malabsorption are also associated with low albumin levels. In addition, as an acute-phase reactant, a low albumin level may simply behave as a marker of an active inflammatory state.

Liver-related disease has become a significant cause of death of patients on long-term ARV therapy.[32] Prolonged survival on ARVs has increased exposure to the following:

- Persistent liver damage resulting from uncontrolled hepatitis B or C virus infection.[33]
- Non-alcoholic steatohepatitis (NASH) may result from HIV infection itself and from exposure to the metabolic side-effects of the ARVs.[34,35]
- Direct drug toxicity. All drugs are potential hepatotoxins but certain ARVs are more frequently associated with liver toxicity, e.g. nevirapine in women with CD4 counts > 250 cells/µl and men with CD4 counts > 400/µl, the combination of stavudine and didanosine, and the protease inhibitor ritonavir.[32,35,36]

Elevated transaminases, e.g. ALT, may accompany liver damage and must be checked two or three times a year while on the

NUTRITIONAL ASSESSMENT OF THE HIV-INFECTED PATIENT[7]

History	Examination	Laboratory tests (baseline assessment and as indicated clinically thereafter)
Weight loss Dietary history Access to food and food security Stage of HIV infection Use of medication including the antiretrovirals Pregnancy, lactation and the 'child under 5' Micronutrient and vitamin use Family and/or community support	Weight Height or length Body mass index (BMI) (normal value: 18.5 - 24.9 kg/m^2) Mid-upper arm circumference (MUAC) (normal values: adult males > 23 cm; adult females > 22 cm; pregnant females > 23 cm) Waist circumference, 'at risk values' (adult males ≥ 102 cm, adult females ≥ 88 cm) Clinical examination of the patient: signs of wasting, evidence of stunting in children, signs of advanced HIV infection, signs of specific nutritional deficiency syndromes, signs of treatment-related fat redistribution	Full blood count and haemoglobin (anaemia) Serum iron studies only if significantly anaemic, Hb < 8 - 10 g/dl otherwise clinically indicated Viral hepatitis serologies (HBV, HCV) and additional liver tests as clinically indicated Plasma fasting cholesterol and triglyceride Plasma fasting blood glucose The albumin level, and specific micronutrient levels are not routinely assessed Serum amylase not routinely assessed
What to do?		
History: Identify food insecurity Assist families/patients with accessing government support and welfare grants Identify lack of nutritional knowledge Refer to counsellor to assist with practical support of the mother/ child/patient Identify a responsible home or community member who can assist Identify opportunities to prevent HIV transmission Assist the pregnant patient with making informed choices including exclusive breastfeeding Where weight loss is confirmed, examine and investigate to exclude opportunistic disease, e.g. tuberculosis, advanced HIV	*Examination* Weight loss is significant and is associated with mortality in the HIV infected. Check measurements to exclude significant weight loss and malnutrition (weight, BMI) Lower than normal MUAC levels: loss of lean body mass Correct underlying malnutrition and ensure virus is brought under control Assess food access, intake and utilisation Examine patient to exclude active opportunistic disease and uncontrolled HIV infection Increased abdominal circumference: check which ARVs are being used and confirm metabolic abnormalities with appropriate investigations Give dietary advice and refer where available to dietician Weight reduction and exercise programme may be indicated	*Laboratory tests* Anaemia, low serum albumin levels indicate an increased risk of death in the HIV infected. All abnormal investigations must be explained and acted upon Anaemia: check the MCV and find the likely cause and correct this Serum iron, % saturation, transferrin and ferritin levels may be helpful if iron deficiency is suspected Elevated ALT: check the AST, alkaline phosphatase, GGT and HBV, HCV antibody tests. Decide whether this is a medication-related toxicity or an opportunistic process. If necessary follow up with a hepatic ultrasound to exclude a space-occupying lesion, fatty liver or NASH, enlarged abdominal lymph nodes

ARVs. Elevated transaminases ought to direct the physician to excluding alcohol (GGT>>AST >>ALT) and the activity of the hepatitis viruses (HBV and HCV) as possible causes.[37,38] Elevated alkaline phosphatise and gamma-gluteryl transferase (GGT) may suggest an infiltrative process including the presence of hepatic granulomas, e.g. TB or cotrimoxazole-induced hepatitis.[39]

2.3.4 Miscellaneous tests

Amylase levels are checked in symptomatic patients with suspected pancreatitis: abdominal pain, nausea, vomiting while taking didanosine or the combination of didanosine and stavudine, and rarely, lamivudine in children. Concomitant use of alcohol, pentamidine, hydroxyurea and steroids including anabolic steroids, will increase the risk.[40] Serum amylase is not tested routinely.

Fasting plasma cholesterol and triglycerides, glucose (or urine dipstix) are suggested at baseline assessment and annually in patients with known risk factors for cardiovascular disease, diabetes, etc. Patients on ARVs associated with lipodystrophy are at an increased risk of cardiovascular disease and insulin resistance. These will also need annual or bi-annual fasting lipids and sugars.[4]

2.4 NUTRITION: THE CLINICAL ASSESSMENT

See also Appendices 1 and 2.

The assessment of the nutritional status of HIV-infected patients begins with the initial interview. A clinical examination follows. This is combined with measurements that are repeated during subsequent follow-up visits: weight, height/length to enable a BMI measurement to be made, MUAC, and in patients on lipid-altering ARVs, waist

circumference can be considered. Baseline and follow-up blood and urine tests complete the assessment and permit clinical staging of the patient. At this time the patient will want to know whether ARV drugs are needed and what if any, is the role of diet, micronutrient supplements and vitamins. These topics will be addressed in the next chapter.

The following chapters of this Guideline will appear in subsequent issues of the *Journal*.

REFERENCES

1. Shevitz AH, Knox TA. Nutrition in the era of highly active antiretroviral therapy. *Clin Infect Dis* 2001; 32: 1769-1775.
2. Truswell AS. Measuring nutrition. *BMJ* 1985; 291: 1258-1262.
3. Nerad J, Romeyn M, Silverman E, *et al*. General nutrition management in patients infected with human immunodeficiency virus. *Clin Infect Dis* 2003; 36 (Suppl 2): S52-62.
4. Grinspoon S, Carr A. Cardiovascular risk and body-fat abnormalities in HIV-infected adults. *N Engl J Med* 2005; 352: 48-62.
5. Souba WW. Nutritional support. *N Engl J Med* 1997; 336: 41-48.
6. Young H, Borrel A, Holland D, Salama P. Public nutrition in complex emergencies. *Lancet* 2004; 364: 1899-1909.
7. Knox TA, Zafonte-Sanders M, Fields-Gardner C, Moen K, Johansen D, Paton N. Assessment of nutritional status, body composition and human immunodeficiency virus-associated morphologic changes. *Clin Infect Dis* 2003; 36 (Suppl 2): S63-68.
8. Jones JM. The methodology of nutritional screening and assessment tools. *J Hum Nutr Dietet* 2002; 15: 59-71.
9. Arpadi SM. Growth failure in HIV-infected children. WHO Consultation on Nutrition and HIV/AIDS in Africa: Evidence, lessons and recommendations for action. Durban, 10-13 April 2005. Geneva: World Health Organization, 2005: 4.
10. Hadigan C, Meigs JB, Corcoran C, *et al*. Metabolic abnormalities and cardiovascular disease risk factors in adults with human immunodeficiency virus infection and lipodystrophy. *Clin Infect Dis* 2001; 32: 130-139.
11. American Dietetic Association. *HIV/AIDS Medical Nutrition Therapy Protocol: Medical Nutrition Therapy Across a Continuum of Care.* Chicago, Ill.: American Dietetic Association, 1998.
12. Heller LS. Nutrition support for children with HIV/AIDS. *J Am Diet Assoc* 1997; 97: 473-474.
13. Weinberg GA, Boelaert JR, Weinberg ED. Iron and HIV infection. In: Friis H, ed. *Micronutrients and HIV Infection*. Boca Raton: CRC Press, 2001: 135-157.
14. Weiss G, Goodnough LT. Anemia of chronic disease. *N Engl J Med* 2005; 352: 1011-1023.
15. Boelaert JR, Weinberg GA, Weinberg ED. Altered iron metabolism in HIV infection: mechanisms, possible consequences and proposals for management. *Infect Agents Dis* 1996; 5: 36-46.
16. Gangaidzo IT, Moyo VM, Mvundura E, *et al*. Association of pulmonary tuberculosis with increased dietary iron. *J Infect Dis* 2001; 184: 936-939.
17. Spivak JL. The blood in systemic disorders. *Lancet* 2000; 355: 1707-1712.
18. Feldman JG, Goldwasser P, Holman S, DeHovitz J, Minkoff H. C-reactive protein is an independent predictor of mortality in women with HIV-1 infection. *J Acquir Immune Defic Syndr* 2003; 32: 210-214.
19. Munford RS. Statins and the acute-phase response (Editorial). *N Engl J Med* 2001; 344: 2016-2018.
20. Tomkins A. Assessing micronutrient status in the presence of inflammation. *J Nutr* 2003; 133; 1649S-1655S.
21. Grunfeld C, Feingold KR. Metabolic disturbances and wasting in the acquired immunodeficieincy syndrome. *N Engl J Med* 1992; 327: 329-336.
22. Halliwell B, Gutteridge JM. The antioxidants of human extracellular fluids. *Arch Biochem Biophys* 1990; 280: 1-8.
23. Nike E. Antioxidants in relation to lipid peroxidation. *Chemistry and Physics of Lipids* 1987; 44: 227-253.
24. Brown KH *et al.* Potential magnitude of the misclassification of a population's trace element status due to infection: example from a survey of young Peruvian children. *Am J Clin Nutr* 1993; 58: 549-554.
25. Eley BS, Sive AA, Abelse L, Kossew G, Cooper M, Hussey GD. Growth and micronutrient disturbances in stable, HIV-infected children in Cape Town. *Ann Trop Paediatr* 2002; 22: 19-23.
26. Visser ME, Maartens G, Kossew G, Hussey GD. Plasma vitamin A levels in HIV infected adults in Cape Town, South Africa. *Br J Nutr* 2003; 89: 475-482.
27. Bobat R, Coovadia H, Stephen CV, *et al.* Safety and efficacy of zinc supplementation for children with HIV-1 infection in South Africa: a randomised double-blind placebo-controlled trial. *Lancet* 2005; 366: 1862-1867.
28. Coutsoudis A, Bobat R, Coovadia H, Huhn L, Tsai W, Stein Z. The effects of vitamin A supplementation on the morbidity of children born to HIV infected women. *Am J Public Health* 1995; 85: 1076-1081.
29. Truswell AS. Levels and kinds of evidence for public-health nutrition. *Lancet* 2001; 357: 1061-1062.
30. Nichol C *et al.* Changes in the concentrations of plasma selenium and selenoproteins after minor elective surgery: further evidence for a negative acute phase response? *Clin Chem* 1998; 44: 1764-1766.
31. Lawlor DA, Smith GD, Bruckdorfer KR, Kundu D, Ebrahim S. Those confounded vitamins: what can we learn from the differences between observational versus randomised trial evidence? *Lancet* 2004; 363: 1724-1727.
32. Morcroft A, Soriano V, Rockstroh J, *et al*. Is there evidence for an increase in the death rate from liver-related disease in patients with HIV? *AIDS* 2005; 19: 2117-2125.
33. Bonacini M, Louie S, Bzowej N, Wohl AR. Survival in patients with HIV infection and viral hepatitis B or C: a cohort study. *AIDS* 2004; 18: 2039-2045.
34. Pol S, Lebray P, Vallet-Pichard A. HIV infection and hepatic enzyme abnormalities: Intricacies of the pathogenic mechanisms. *Clin Infect Dis* 2004; 38 (Suppl 2): S65-72.
35. Duval X, Journot V, Leport C, *et al*. Incidence and risk factors for adverse drug reactions in a prospective cohort of HIV-infected adults initiating protease inhibitor-containing therapy. The Antiprotease Cohort, APROCO. *Clin Infect Dis* 2004; 39: 248-255.
36. Van Leth F, Andrews S, Grinszteyn B, *et al.,* for the 2NN Study Group. The effect of baseline CD4 cell count and HIV-1 viral load on the efficacy and safety of nevirapine or efavirenz-based first-line HAART. *AIDS* 2005; 19: 463-471.
37. Pratt DS, Kaplan MM. Evaluation of abnormal liver-enzyme results in asymptomatic patients. *N Engl J Med* 2000; 342: 1266-1271.
38. Kew M. Serum aminotransferase concentrations as evidence of hepatocellular damage. *Lancet* 2000; 355: 591-592.
39. Kreisberg R. Clinical problem solving. *N Engl J Med* 1995; 332: 945-949.
40. Dube M. Disorders of glucose metabolism in patients infected with HIV. *Clin Infect Dis* 2000; 31: 1467-1475.

APPENDIX 1

ENTRY AND EXIT CRITERIA: ADULTS > 14 YEARS

NUTRITION RISK SCORE

If the total score exceeds 6 points, the patient can be seen as nutritionally at risk and requires food and to be provided with long-term nutritional support and access to government or NGO assistance or welfare grants. Where practical, the patient should be referred to a dietician for appropriate nutritional intervention.

	DATE AND SCORE						
1. Weight loss in 3 months							
• None	0						
• 3 kg (< 1clothes size)	1						
• 3 - 6 kg (1 - 2 clothes size)	2						
• > 6 kg (> 2 clothes size)	3						
2. BMI							
• ≥ 18.5	0						
• 17.0 - 18.4	1						
• 16.0 - 16.9	2						
• ≤ 16	3						
3. Appetite							
• Good (most of plate)	0						
• Poor (half of plate eaten)	1						
• Unable to eat (no food in 2 days)	2						
4. Ability to eat							
• No problems	0						
• Mild vomiting/diarrhoea	1						
• Difficult swallowing/chewing	2						
• Severe vomiting/diarrhoea	2						
• Need help feeding	3						
5. Stage of infection (WHO stage classification)							
• Stage I	0						
• Stage II	1						
• Stage III	2						
• Stage IV	3						
6. Other problems							
• None	0						
• TB	2						
• Pregnant/lactation	2						
• Social problems	2						
TOTAL SCORE							

Source: Harman C. Nutritional Assessment Chart. Nutrition Unit, Department of Paediatrics, Chris Hani Baragwanath Hospital, Soweto, 2007.

APPENDIX 2

ENTRY AND EXIT CRITERIA: CHILDREN < 14 YEARS

NUTRITION RISK SCORE

If the total score exceeds 6 points, the child is nutritionally at risk and needs to be given food and provided with long-term nutritional support and access to government or NGO assistance or grants. Where practical, the patient should be referred to a dietician for an appropriate nutritional intervention. Where acute malnutrition is diagnosed, this child MUST BE ADMITTED to hospital and provided with appropriate formula feeding as per WHO guidelines. RTHC = Road to Health Chart.

	DATE AND SCORE					
Is this child malnourished?						
1. Present weight:						
0 - 3 years (RTHC)						
• Following a curve on the RTHC	0					
• Inadequate weight gain, growth faltering	2					
• ≤ 3rd percentile RTHC	4					
• ≤ 60% of expected weight on the RTHC	6					
2 - 14 years BMI						
• ≥ 50th percentile	0					
• < 50th percentile	2					
• ≤ 25th percentile	4					
• < 3rd percentile	6					
3. Appetite						
• Good (5 meals a day)	0					
• Poor (less than 3 meals daily)	2					
• Unable to eat (no food in 2 days)	4					
4. Ability to eat						
• No problems	0					
• Mild vomiting/diarrhoea	1					
• Difficult swallowing/chewing	2					
• Severe vomiting/diarrhoea	4					
5. Stage of infection						
• Stage I	0					
• Stage II	1					
• Stage III	2					
• Stage IV	3					
6. Other problems						
• None	0					
• TB	2					
• Pregnant/lactation	2					
• Social problems	2					
TOTAL SCORE						

Source: Harman C. Nutritional Assessment Chart. Nutrition Unit, Department of Paediatrics, Chris Hani Baragwanath Hospital, Soweto, 2007.