

## Aspects of body composition in human immunodeficiency virus (HIV) infection

C.J. Oliver<sup>\*</sup>, B.J. Allen<sup>†</sup> and J. Gold<sup>\*</sup>

<sup>\*</sup>Albion Street Centre, Department of Medicine, Prince of Wales Hospital, Surry Hills, NSW, Australia; <sup>†</sup>St George Hospital Cancer Care Centre, Kogarah, NSW

In the mid-1980s, body composition studies of symptomatic AIDS patients, utilizing total body potassium counting and isotope dilution, indicated that the pattern of weight loss observed in advanced HIV infection was similar to a stressed or injured state, rather than one of starvation. A disproportionate depletion of body cell mass (of which skeletal muscle is a major component), relative to loss of body weight, was seen along with a relative expansion of the extracellular fluid volume. The same researchers observed that this decline in body cell mass was predictive of mortality. Cross-sectional studies in HIV infection have also indicated that a reduction in body cell mass can occur early in the disease process; these studies utilising bioelectrical impedance analysis as a means of body composition assessment.

### Introduction

Human immunodeficiency virus (HIV) infection has justifiably been called a paradigm of malnutrition. The virus progressively destroys the immune system as well as affecting all organ systems, therefore it is not surprising that a number of diseases and symptoms with nutritional implications can become evident. Indeed weight loss and nutrient deficiencies, often interrelated with diarrhoea, malabsorption and fever, are common symptoms of HIV disease. The primary nutritional problem encountered in advanced HIV disease is weight loss which is characteristic of at least 90% of acquired immunodeficiency syndrome (AIDS) cases and believed to be a significant contributor to morbidity and mortality. Weight loss in HIV disease has many causes including opportunistic infections and fever, malabsorption, as well as malnutrition due to apathy and social deprivation. Significantly, weight loss may occur in the absence of any secondary infections, the human immunodeficiency virus itself been proposed as a major contributing factor.

### Epidemiology

Human immunodeficiency virus (HIV) infection is a global epidemic. As of 30 June 1993 although approximately 720 000 cumulative AIDS cases of adults and children had been reported to WHO, the actual number was estimated as closer to 2.5 million cumulative AIDS cases<sup>1</sup>. The estimated global cumulative cases of HIV infections in adults in mid-1993 was greater than 13 million; approximately 8 million of which are in Sub-Saharan Africa and 1.5 million in South-East Asia.

The precise details of the course from HIV infection to immune deficiency are poorly understood. The time from HIV seroconversion to the onset of AIDS may take 10 years; the exact length of time will vary within and between patient demographics' ie male, female, adult, child, IVDU, homosexual, heterosexual, transfusion recipient, African, European, etc. . . . Individual clinical patterns over the entire disease spectrum will also vary. Superimposed on this is the

tremendous amount of official and unofficial experimentation in drug treatments for HIV infection that has occurred in the last five years. Treatment and illness characteristics may actually change within a population group within a relatively short period of time. Even more importantly is the increasing evidence that the intervening period between the two clinical landmarks of seroconversion and 'AIDS' is not as benign as first thought. Viral, biochemical, metabolic and body composition changes reported in the 'latent' or 'asymptomatic' phase of HIV infection, mean that currently used reference points for disease staging in early HIV infection may be inadequate. Given the considerable heterogeneity in the HIV disease spectrum and patient demographics, it may be invalid to simply extrapolate data from one environment to another.

### Weight loss and body composition

The problems of HIV disease staging and patient demographics certainly also apply when assessing body composition studies in HIV infection. For example 'slim' disease in Africa and HIV 'wasting' syndrome in western countries, are not duplicate clinical identities. Additionally at the individual study level, the heterogeneity in disease patterns may also confound outcomes; cross-sectional comparison of measurements across different stages of HIV infection, based on what are predominantly CDC epidemiological surveillance classifications, may be particularly susceptible to this effect.

Notwithstanding, we do have insights into the body composition changes of HIV infection. The first and still most detailed assessment of body composition in advanced HIV infection was done in the mid-1980s by researchers at St Lukes-Roosevelt Hospital, New York<sup>2</sup>. Detailed body composition studies were performed in 33 (26 m, 7 f) HIV-positive persons, 28 with CDC classifications for AIDS and five with AIDS-related complex (ARC). Fourteen of the AIDS

patients and one of the ARC patients had diarrhoea. Total body potassium (TBK) was measured in a 4- $\pi$  whole body liquid scintillation counter and expressed as potassium (meq)/height (cm) (K/ht) before being normalized by age and sex; % body fat was estimated by the Steinkemp formula (1965). Total body water (TBW) and extracellular water (ECW) were measured by the  $^3\text{H}_2\text{O}$  and  $^{35}\text{SO}_4$  isotope dilution methods, respectively, and intracellular water (ICW) determined by difference. The immunodeficient group were observed to be  $82\pm 10\%$  of ideal weight (1963 Metropolitan Life Insurance Tables), but only  $68\pm 10\%$  K/ht of the idealized subject. Whereas the degree of potassium depletion was similar for males and females, in patients with diarrhoea the degree of potassium depletion was significantly greater than those without diarrhoea, ie  $62\pm 9\%$  vs  $74\pm 9\%$ . The immunodeficient group were also found to be depleted of body fat when compared to normal values, but similar to homosexual controls. Even though the ratio of TBW/ht was decreased, the ratio of TBW/wt was increased and paralleled by a relative increase in ECW. Female patients had strikingly less body fat per body wt (% of normal), compared to male patients ( $29\pm 30\%$  vs  $71\pm 21\%$ ), similar to that seen in females with eating disorders, but also less severe TBK depletion. It should be noted that most of the female patients had oropharyngeal and/or oesophageal candidiasis which inhibited food intake, but fewer serious disease complications. On the other hand, the male patients were said to have significant TBK depletion relative to body fat depletion. It was concluded that, whereas the pattern of weight loss in the female patients was similar to anorexia nervosa and marasmus, in the male patients the pattern 'resembled that of a stressed or injured state rather than simple starvation'.

In a subsequent paper by the same group, the relationship between death from wasting and the magnitude of body cell mass depletion was examined<sup>3</sup>. Data was presented on 32 HIV-positive patients who were evaluated within 100 days of dying from wasting illness. Body cell mass (BCM) and body fat were again estimated by TBK and anthropometric measurement, with weight and TBK/ht again normalized. Forty-three assessments were performed, seven of these postmortem and the data were plotted as a function of time before death and analysed by regression. The extrapolated normalized TBK at death was 54% and for body wt 60% of ideal, while at 100 days prior to death, body wt was 90% of ideal and TBK 71% of normal. No significant linear relationship was found when 'body fat contents' were plotted. It was concluded that BCM wasting occurred independent of changes in body fat and that these changes were likely to be related to the relative increases in ECW that had been previously described.

The method of total potassium counting to measure BCM may be affected by acute illnesses and especially by diarrhoea<sup>4</sup>. Reduced TBK measurements in patients with diarrhoea possibly reflect the extent of disease activity and potassium imbalance rather than the actual loss of BCM. Secondly, use of idealized weight and TBK/ht indices may have overestimated the degree of depletion, as the usual weight of the presumably male homosexual population may be less than the calculated ideal of the general population. Nevertheless the body water (TBW, ECW) data do support the overall conclusion regarding the nature of the body composition changes. Using *in vivo* neutron capture analysis as a measure of BCM, the body composition of a group of 'asymptomatic' seropositive men was compared to another

group of men with moderate to severe HIV-related weight loss (see Table 2). In Allen BJ, et al. Role of body protein as a prognostic indicator in wasting disease, this issue<sup>5</sup>. No disproportionate loss in body nitrogen could be observed relative to other body compartments. However, re-analysis of the data assuming that only approximately two-thirds of the total body nitrogen is metabolic, did show a disproportionate loss of nitrogen in the weight loss group which agreed with Kotler's observations.

However, from clinical experience we know that weight loss can occur in the absence of secondary infections and can be one of the first signs of advancing HIV disease. In a cross-sectional study that utilized the bio-electrical impedance measurement of body composition, 340 control subjects were compared with 193 HIV seropositive persons who were staged by the Walter Reed system — 26 subjects were in WR2 (early HIV infection), 85 in WR3-5, and 82 in WR6<sup>6</sup>. Despite there being no difference in age, height or weight between the control group and WR2 group, resistance ( $465.4\pm 61.2$  vs  $492.3\pm 49.1$ ) and reactance ( $54.5\pm 7.8$  vs  $49.6\pm 8.2$ ) were already significantly higher and lower, respectively, in the WR2 subjects. These results were indicative of a significant reduction in BCM and an increase in extracellular mass (ECM) and ECM/BCM ratio in early HIV infection. The more advanced WR3-5 and WR6 groups also had significantly increased resistance measurements and decreased measures of reactance compared to controls, but significant decreases in weight as well.

Nevertheless, there have been very few detailed studies that have assessed longitudinal changes to body composition in HIV infection. In a group of 'asymptomatic' HIV seropositive men no changes in total body nitrogen as measured by *in vivo* neutron capture analysis, were observed over an 18-month period in which the subjects' immune function and weight remained stable (see Table 3. Allen et al. BJ, Role of body protein as a prognostic indicator in wasting disease, this issue). However, detailed anthropometry performed on this cohort using data over a longer time period did observe an apparent loss of lower limb muscle. This loss occurred in the absence of serious HIV-related clinical symptoms (including weight loss) and independent of CD4 T lymphocyte function and anti-retroviral medication. An important question is what would cause this loss of muscle in an otherwise overtly healthy population. It has been postulated that HIV-stimulated cytosine, eg TNF, IL-1, etc, activity could be responsible. However, in a recent review Grunfeld<sup>8</sup> argues that as an adaptation to an increase in resting energy expenditure, which could happen in early HIV infection, a decrease in physical activity could occur with a resultant loss of weight and muscle. The onset of opportunistic infections would cause an acceleration of pre-existing muscle wasting. However in the longitudinal cohort data previously mentioned, loss of muscle appeared to occur despite normal to high levels of physical activity.

## Conclusion

There is increasing evidence that depletion of body cell mass may be an early manifestation of HIV infection. This and other evidence challenge the concept of a benign latency period prior to the onset of AIDS-defining symptoms. Follow-up longitudinal body composition studies with adequate subject numbers that can address all the issues of population and disease heterogeneity are required. However given the relatively rapid changes in treatment regimes, including

impending vaccine trials, this may be difficult to do so. Regardless, as the majority of the world's HIV seropositive persons live in economically disadvantaged conditions, it is important to continue to validate low cost and 'low-tech' options of body composition assessment.

### References

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