HIV - IMPLICATIONS FOR EXERCISE IN TREATMENT AND REHABILITATION

ABSTRACT: Exercise is an integral part of many forms of rehabilitation following muscle injury or surgery. It is usual to advise patients with a viral infection to avoid exercise because of the risk of developing myocarditis. Should HIV+ patients should be encouraged to undertake exercise as part of rehabilitation and should they further be advised to participate in regular exercise? There is sufficient evidence to support the benefits of regular exercise in the HIV+ patient. They will experience a training effect dependent on the normal parameters of frequency, intensity, duration, and mode of exercise. The disease does place potential limitations to exercise, as the HI virus directly affects pulmonary, cardiac, skeletal muscle and endocrine function. The effects of these changes may be exacerbated by secondary infection and other pathological changes may be induced by treatment. The advent of highly active antiretroviral therapy has brought with it a range of metabolic changes that may also influence exercise participation. The limitations to exercise imposed by HIV infection and its treatment are reviewed.

KEY WORDS: HIV, EXERCISE, LUNG FUNCTION, CARDIAC FUNCTION, SKELETAL MUSCLE, METABOLIC DISTURBANCE.

It is currently estimated that there are over 50 million people in the world infected with the human immune deficiency virus (HIV). This constitutes about 0.8% of the world’s population. Two thirds of the cases are in sub-Saharan Africa and about 10,000 people die each day of AIDS and its complications on this continent. Botswana has the dubious distinction of having the highest percentage of its population infected. South Africa has the most HIV positive people, approximately 4.5 million, with over a 1000 people dying daily of AIDS. Based on antenatal clinic attendance data, KwaZulu Natal is hardest hit in South Africa, with about a third of its population infected. It is sobering to note that in its 2002 update, the United Nations Population Division still predicts that the population of Africa will increase two and half fold by 2050, and that the population of South Africa will decrease by 8%.

The disease does not appear to be coming to a natural end. It is forecast that the epicentre of the disease will move from southern Africa to West Africa and then to India and that it will only peak in 40 to 60 years time.

As the HIV/AIDS pandemic continues, the pattern of the disease is changing. In the developed world, the advent of highly active antiretroviral therapy (HAART) has improved CD4 counts and reduced viral loads. As a result there is a reduction in opportunistic infection and the disease is being converted into a chronic illness. This partial success in the management if HIV/AIDS is not without cost, as the incidence of treatment associated or induced pathology, like lipodystrophy, increases. There are now reports of increasing ischaemic heart disease, stroke, glucose intolerance, diabetes and lactic acidosis in those on HAART.

In much of the developing world, where HAART is not freely available, the disease profile remains unchanged, with opportunistic infection and muscle wasting the features of the disease.

Knowing or unknowingly, physiotherapists are treating HIV+ patients daily, for conditions ranging from chest infections to muscle pain. It is stated that 76% of HIV+ positive people in South Africa did not know that they are infected and of these, 63% did not know that they were at risk (Shisana 2003).

The aim of this paper is to raise awareness and understanding of HIV/AIDS by reviewing the disease process, the principles of treatment, the effects of the disease on cardiopulmonary and skeletal muscle function and the effect of treatment on the body. The possible use of exercise as a treatment or rehabilitation modality will be discussed.

Data were acquired by searching the Medline and AIDSlit databases using the exploded keywords, HIV, AIDS, exercise and exertion. Using the Boolean command OR, HIV and AIDS were combined and exercise and exertion were combined. The two new subsets were then combined using the Boolean command AND to derive a search of HIV/AIDS AND Exercise/Exertion. Further searches were conducted of HIV/AIDS AND Cardiac function/cardiac function testing, HIV/AIDS AND skeletal muscle, HIV/AIDS AND pulmonary function/pulmonary function testing, HIV/AIDS AND anabolic steroids, and HIV/AIDS And Metabolism. This yielded 2252 papers. All papers in English on HIV/AIDS and exercise were acquired and reviewed and additional papers referenced in these papers were reviewed. All the abstracts of the other searches were read and the full papers of those

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after infection and act as a reservoir or "viral manufacturing plant". Monocyte function is affected, with defective chemotaxis, reduced ability to kill target cells such as parasites, and reduction in production of Interleukin-1 (Lawless et al 1995, Talle et al 1983).

The Natural Killer cell (NK), which plays an important role in immune surveillance against tumour cells and viruses in non-specific natural immunity, is also affected. While NK cell numbers are not greatly affected in AIDS, their cytotoxicity is significantly reduced early in the disease process (Rosenberg and Fauci 1990, Talle et al 1983).

After primary infection, the disease enters a latent phase during which its presence in the extracellular fluids is low and relatively few CD4 cells are infected. The disease is not however quiescent and continues in the lymph nodes, where the virus multiplies in macrophages, follicular dendritic cells and in up to 10 % of the CD4 cells (Pantaleo et al 1993, Rutherford et al 1990). The patients are usually asymptomatic in this phase and they are relatively healthy. During this phase they can transmit the disease and their immune system is compromised. As the disease progresses patients may develop symptoms such as fatigue, intermittent fever, lymphadenopathy, weight loss and diarrhoea as fatigue, intermittent fever, lymphonephadenopathy, weight loss and diarrhoea without major opportunistic infections or cancer. This is known as the AIDS related complex. Eventually most patients will be diagnosed with AIDS, either due to and infected cells and the production of Interleukin-1 (Lawless et al 1995, Talle et al 1983).

The HIV virus also infects monocytes, the cells responsible for the presentation of antigens to the T cells. The HI virus enters monocytes largely through phagocytosis and not through gp120-CD4 binding, although some monocytes do express the CD4 receptor. Unlike the CD4 cells, the monocytes do not die a "false" viral DNA. An example of this is zidovudine, or AZT. Non nucleoside reverse transcriptase inhibitors like nevirapine, competitively block reverse transcriptase. The host cells ribonucleotide production can also be blocked by ribonucleotide reductase inhibitors. The protease inhibitors block the cleavage, packaging and release of the newly formed viral RNA and viral proteins.

Monitoring the course of the disease in HIV+ patients is usually done by following changes in CD4 counts or more recently viral load. There has been much debate on whether exercise raises CD4 counts, stabilises them, or slows the rate of decline. To interpret the data one needs to know the normal response of T lymphocytes to exercise in both the uninfected and infected individual. In addition the variability of the CD4 count test must be taken into account when drawing conclusions based on CD4 counts.

Exercise induces both neutrophilia and lymphocytosis during exercise. After exercise the neutrophilia persists while lymphopaenia develops, with lymphocyte counts dropping to below pre-exercise values. The increase of the lymphocyte subsets differs during exercise with CD16 Natural Killer cells showing the greatest increase and CD4 cells undergoing a relatively small increase. Natural killer cell and lymphokine activated killer cell (LAK) activity is increased during and immediately after exercise of moderate intensity and duration (Pedersen et al 1998). In HIV+ patients subjected to 1 hour of exercise at 75 % VO2max on a cycle ergometer, lymphocyte responses to exercise and recovery were similar to that of controls but the level of elevation of the lymphocyte subsets during exercise was decreased. Similarly, NK and LAK activity during and after activity was less than that of controls (Ullum et al 1994).

As the CD4 count is used as an indicator of the possible benefits of exercise in HIV+ patients, the important observations on the variability of CD4 counts made by Raboud et al need to be detailed (Raboud et al 1995). They emphasised the need to know the co-efficient of variation of the test in different labs. In their own lab, repeat tests on the same
sample had a coefficient of variation of 13.7 % with the median difference between 2 tests of 16 cells.mm^{-2}. While this may appear to be an acceptable variation, the maximum difference was 105 cells.mm^{-2}. They concluded that in their lab, a change of more than 27 % would be required in the short term to be confident that a meaningful change has occurred.

In summary, the CD4 cells are infected and lose their function of signalling other cells in the immune system to mount adequate cellular and humoral immune responses. Natural immunity is impaired because of the failure of monocytes and NK cells to provide immune surveillance against parasites, other pathogens and tumour cells and their inability to produce normal concentrations of cytokines, results in a breakdown of cell to cell signalling. The clinical course of the disease can be monitored by the falling CD4 count and rising plasma viral load.

STAGING OF THE DISEASE
The two most commonly cited classifications of the disease are the Walter Reed Staging and Centre for Disease Control (CDC) classification (Tables 1 and 2).

EXERCISE AND HIV
Oxygen Uptake, Delivery and Consumption
Patients with HIV infection who do not have full blown AIDS or pulmonary infection have reduced work capacity, lower aerobic threshold, and poorer aerobic capacity than age matched controls (Johnson et al 1990, Keyser et al 2000, Roge et al 2002, Smith et al 2001). Oxygen consumption during exercise is dependent on its uptake from the lungs, delivery by the heart and blood and its utilisation by skeletal muscle. These will be addressed separately.

PULMONARY FUNCTION
The Effect of the Disease on the Lungs
The lungs are a common site of secondary or opportunistic infection in HIV/AIDS, but the HI virus also has a direct effect on the lung physiology. Reduction in diffusion capacity without overt lung disease is a common pulmonary feature of HIV infection (Kvale et al 1993, McCabe et al 1997). This worsens with time and a diffusion capacity of <80 % predicted is associated with a more rapid progression of the disease to AIDS (Nieman et al 1993). In addition, most lung function tests are abnormal in the HIV+ population.

Decreased diffusion capacity is associated with reduced pulmonary capillary blood volume, well-preserved total lung capacity and no evidence of interstitial fibrosis. There is evidence of early emphysema and focal air trapping, the severity of which correlates with diffusion capacity (Diaz et al 1999). Associated with this are significant reductions in mean FEV1 and forced mid-expiratory flow (Gelman et al 2000). Bronchial dilatation may also be present and this has been linked to increased neutrophil concentrations found on bronchoalveolar lavage (King et al 1997). The concentration of the antioxidant glutathione found in the respiratory epithelial lining fluid is reduced in HIV+ subjects and the concentration falls with time (Pacht et al 1997).

Exercise and Lung Function
Johnson et al. compared pulmonary function at rest and during exercise in 32 HIV+ soldiers, without AIDS and with no overt or pre-existing pulmonary or cardiac disease, with an age matched control group. The HIV+ subjects complained of dyspnoea on exertion or difficulty with mandatory exercise. While pulmonary function tests were normal, patients exercised to a significantly lower workload and had a significantly lower anaerobic threshold. Maximal oxygen consumption (VO_{2max}) and minute ventilatory volume were non-significantly lower, and maximal heart rates were similar. The slope of the heart rate vs VO_{2} relationship was increased indicating that the heart rate of the patients was greater than that of the controls at any given oxygen consumption. They concluded that some seropositive patients have impairment in maximal exercise capability and that there was no evidence that this was due to a ventilatory limitation. They felt that the findings were consistent with a problem of oxygen delivery to the muscles secondary to cardiac problems. It should be noted however that only one subject had a mild reduction of single breath, oxygen diffusion capacity (Johnson et al 1990).

Pulmonary function is affected by repeated bouts of pneumonia which reduce pulmonary diffusing capacity,

Table 1: Walter Reed Classification.

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<th>Walter Reed Classification</th>
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<tr>
<td>WR 1 CD4 count ≥ 400.mm^{-2}, no signs or symptoms,</td>
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<td>WR 2 CD4 count ≥ 400.mm^{-2}, lymphadenopathy present,</td>
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<tr>
<td>WR 3 CD4 count &lt; 400.mm^{-2}, normal delayed hypersensitivity,</td>
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<tr>
<td>WR 4 CD4 count &lt; 400.mm^{-2}, partial cutaneous anergy</td>
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<tr>
<td>WR 5 CD4 count &lt; 400.mm^{-2}, complete cutaneous anergy or oral thrush present</td>
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<td>WR 6 CD4 count &lt; 400.mm^{-2}, opportunistic infection present</td>
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Table 2: Centre for Disease Control coding for AIDS.

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<td>A Asymptomatic. Patient able to transmit the disease and immune function compromised.</td>
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<td>B Early symptomatic pre-AIDS. Fever and or diarrhoea persisting more than 1 month, involuntary weight loss and or a diagnosis of an infectious disease associated with HIV-1 and indicative of a defect in cell mediated immunity</td>
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<td>C AIDS. CD4 count &lt; 200.cells.mm^{-2} and or the presence of a major complication such as an opportunistic infection or malignancy</td>
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ventilatory volume, oxygen consumption and oxygen pulse during exercise. The initial effect of this is haemoglobin desaturation during vigorous exercise, which develops into desaturation with light exercise. Exercise induced desaturation is used as a simple test to diagnose *Pneumocystis carini* pneumonia (PCP) in HIV+ patients (Chouaid et al 1995).

The effects of pneumonia on pulmonary function in HIV/AIDS have been examined by Pothoff et al, who performed pulmonary function and cardiopulmonary exercise tests on three groups of HIV+ and AIDS patients. Subjects in group 1 had not had pneumonia, those in group 2 had just recovered from PCP pneumonia, and group 3 had a current chest infection. They were compared with an HIV-control group, free of pulmonary infection. All HIV+ groups had reduced oxygen diffusing capacity and reduced exercise capacity compared to controls. Lung function assessed by spirometry was significantly reduced in group 3 and oxygen diffusion capacity was significantly reduced between groups. Heart rate at any given oxygen consumption increased from group 1 to 3. Similarly oxygen consumption at anabolic threshold, peak VO₂ and oxygen pulse decreased from group 1 to 3. Alveolar arterial oxygen difference was also significantly greater during exercise in group 3. They concluded that HIV infection is associated with impairment of diffusing capacity and exercise capacity and questioned whether the problem was in oxygen delivery or muscle utilisation (Pothoff et al 1994).

**The Effect of HIV on Heart.**

Resting heart rate is elevated in HIV infection and this is attributed to an increase in resting energy expenditure due to high viral load, HAART, night sweats, fever and secondary infection (Shevitz and Knox 2001a). Cardiac pathology is evident early in the disease. Cardiac abnormalities have been reported in 25 - 73 % of HIV+ adults, and are found at autopsy in two thirds of AIDS patients (Steinherz et al 1986). Left ventricular dysfunction and ECG abnormalities are common sequelae (Barbaro et al 1996a, Cardoso et al 1998, Hernandez et al 2001, Herst et al 1991, Milei et al 1998) and the right side of the heart may also be involved (Casalino et al 1996). Cardiac causes of mortality, however, are estimated at only 1 - 6 % (Mehta et al 2002). Pericardial effusion, pericarditis, myocarditis, cardiomyopathy, endocarditis, pulmonary hypertension and cardiac lymphomas are among the many known cardiac manifestations of HIV infection (Duong et al 1997, Milei et al 1998).

The virus appears to have a direct effect on the myocardium and approximately 50 % of AIDS patients have a lymphocytic myocarditis at autopsy for which no specific aetiological factor can be found, (Milei et al 1998) and approximately a quarter of these patients will have had ventricular arrhythmias (Barbaro et al 1996b).

**Effect of Treatment on the Heart**

Changes in ventricular wall thickness appear to be dependent on the stage of the disease and treatment. Protease inhibitors have been linked to increases in posterior wall thickness, septum thickness, left atrial dimension and LV mass and this appears to be related to the duration of treatment (Meng et al 2002). Zidovudine (AZT) has been linked to left ventricular hypertrophy, increased left ventricular mass and increases the risk of cardiomyopathy in children (Domanski et al 1995, Lipshultz et al 1992).

In aids wasting syndrome (AWS) there is a significant reduction in left ventricular mass when corrected for body surface area. This is associated with left ventricular dysfunction (Samaan et al 1995).

Since the advent of HAART, lipid and metabolic disorders have increased in the HIV+ population. Protease inhibitors have been suggested as the cause of atherosclerosis and coronary artery disease in HIV (Bocara et al 2002, Mehta et al 2002). Coronary artery disease is also considered to be increasing and silent myocardial ischaemia has been documented in 11 % of subjects with no cardiac symptoms or history, with a significant correlation between silent infarct and obesity, waist-to-hip ratio, central fat accumulation, and glucose and cholesterol concentrations (Duong et al 2002).

**The Effect of Exercise on the Heart**

Heart rate is raised at rest and during submaximal graded exercise tests but maximum heart rate does not appear to be affected (Johnson et al 1990, Johnson et al 1991). Aerobic training in HIV+ individuals evokes the same responses of reduced heart rate at a given submaximal workload and reduced resting and recovery heart rate seen in the uninfected (Keyes et al 1989, MacArthur et al 1993, Rigby et al 1992). There is limited information on direct studies of the heart during or immediately after exercise.

In a study of 21 patients with AIDS and no history of cardiac symptoms, radionucleotide angiography was performed at rest and after exercise and compared with 12 age matched subjects who also had no history of cardiac disease. Eleven patients had abnormal ECG’s, a third had right ventricular dilatation, and wall motion abnormalities were seen in 9 patients, with the right ventricle affected in 8 of the 9 patients. No dilatation or wall motion abnormalities were seen in the control group. Importantly, the mean left ventricular ejection fraction at rest and after exercise was not different between groups. In 7 of the 15 patients, ejection fraction was unchanged or reduced after exercise (Herst et al 1991).

Nine HIV+ subjects with dyspnoea on exertion, a VO₂max of less than 80 % of predicted, a low ventilatory threshold, no opportunistic infection and no known pre-existing cardiac or pulmonary disease underwent right-sided cardiac catheterisation. They were compared against historical controls. Three of the 9 patients had abnormal ECG’s, and 2 were normal in every respect in terms of non-invasive exercise testing. Catheterisation data revealed that right atrial and pulmonary capillary wedge pressures were higher in the patient group during exercise and pulmonary artery pressure was higher in the patient group at rest but not during exercise. Cardiac output data during rest and exercise were not different between groups. Mixed venous saturation was significantly lower in the patient group at rest and the arterio-venous O₂ content difference was higher. The patients exercised to the same submaximal
workload as the controls and had a similar VO2 max and cardiac index response. This was achieved at higher filling pressures for both the right and left ventricles, a feature indicative of cardiac disease (Johnson et al 1991).

Anaemia
Anaemia is a feature of HIV/AIDS and will affect aerobic exercise performance by reducing oxygen carriage and hence oxygen delivery to working muscle. Anaemia alone may account for the reduction in VO2 max noted in some studies (Pothoff et al 1994, Stringer 2000).

Skeletal Muscle
Muscle is severely affected by AIDS. Illness with decreased physical activity causes deconditioning and muscle atrophy. In addition there are the problems of AIDS wasting syndrome with loss of muscle mass, HIV polyomatisis, Zidovudine therapy induced mitochondrial myopathy and myositis (MacArthur et al 1993, Sheik et al 1999, Stringer 2000). At autopsy, 70 % of AIDS victims show microscopic abnormalities of muscles (Wrzolek et al 1990).

HIV can cause a skeletal muscle myopathy that is associated with progressive proximal weakness, elevated creatine phosphokinase, myofibrillar damage, fibre necrosis, inflammatory infiltrates and lipid droplet accumulation (Bailey et al 1987, Sheik et al 1999, Simpson and Bender 1988). Treatment induced myopathies also occur. Zidovudine, causes a mitochondrial myopathy with ragged-red fibres, fibre necrosis, lipid drop accumulation, increased size and number of mitochondria, disorganisation of cristae and mitochondrial DNA depletion (Sheik et al 1999). This occurs in skeletal muscle but not in cardiac muscle. Associated with this is an increase in plasma lactate concentration (Chariot et al 1999) that has been attributed to nucleoside reverse transcriptase inhibitors (NRTI), inhibiting MTAP. This has been attributed to nucleoside reverse transcriptase inhibitors (NRTI), inhibiting mitochondrial DNA polymerase γ. This inhibits replication of mtDNA that encodes subunits of the enzymes of the respiratory chain. As a result there is reduced oxidative phosphorylation, necessitating increased conversion of pyruvate to lactate to produce ATP for muscle contraction (Aggarwal et al 1996). The myopathy responds well to stopping Zidovudine.

Muscle Loss and AIDS Wasting Syndrome
Maintenance of adequate nutrition can be a problem in HIV infection. Resting energy expenditure is increased by about 10 % in weight stable HIV+ men without active opportunistic disease and may be further raised by illness and or treatment (Heijligenberg et al 1997). Nutritional status is affected by reduced oral intake because of associated nausea, anorexia and oral infection or by reduced absorption because of diarrhoea or malabsorption (Shevitz and Knox 2001b). In many people the deficit in daily energy intake exceeds the energy conserved by reduced physical activity and weight is lost. This should be taken into account when considering adding exercise, with its additional energy demands, to the treatment regimen.

In the early stage of HIV infection, there are minimal changes in body weight. There are however changes in body composition, with body cell mass decreasing and total body water increasing. Subsequent opportunistic infection results in anorexia, negative nitrogen balance and wasting. Muscle mass is severely affected in advanced AIDS. As muscle is the primary reserve of amino acids for gluconeogenesis and protein synthesis, the loss of muscle mass results not only in loss of strength but also loss of substrate (Sattler et al 1999).

The acquired immunodeficiency syndrome wasting syndrome (AWS) is characterised by the loss of lean body mass out of proportion to weight (Kotler et al 1989, Kotler et al 1998). In men it is defined as 10 % weight loss at any time, 5 % weight loss over 6 months or a BMI < 20 kg.m-2 (Roubenoff and Wilson 2001). AWS is associated with low testosterone concentrations and hypogonadism has been reported in up to 50 % of men with AIDS (Dobs et al 1988). Approximately 60 % of women with AWS are also reported to have an androgen deficiency (Grinspoon and Mulligan 2003). Serum androgen concentrations have been shown to correlate with lean body mass in males and females (Grinspoon et al 1996) and loss of lean body mass is associated with decreased survival. Despite the loss of muscle mass, patients with AWS retain the ability to respond to exercise with protein synthesis and exercise induced protein synthesis in AWS may be greater than in HIV+ patients without AWS (Roubenoff et al 2001). Various methods of increasing muscle mass, reducing weight loss and improving strength are resistance training and treatment with androgenic agents that include anabolic steroids, (Bhasin et al 2000, Sattler et al 2002, Strawford et al 1999) recombinant human growth hormone (Corcoran 1998, Grinspoon and Mulligan 2003) and appetite stimulants (Steinhart 2001).

Obesity has been reported in one longitudinal study on patients on HAART, with 5 % of men and 20 % of women having a Body Mass Index > 30 kg/m² (Shevitz and Knox 2001b). The effect of HAART on catastrophic weight loss and AWS is less clear, with some contending that AWS is the AIDS defining condition in >20% of patients and that the incidence of wasting does not appear to be influenced by HAART (Roubenoff and Wilson 2001, Shevitz and Knox 2001b). A recent 8 month longitudinal study reports AWS as low as 2 %, with loss of lean body mass in patients on HAART being related to the actions of catabolic cytokines and not inadequate dietary intake or hypogonadism (Roubenoff et al 2002a).

Exercise can play a role in the treatment of both those who have wasting and the obese. Strength training associated with adequate nutritional intake is associated with increased lean muscle mass (Fairfield et al 2001) and combined aerobic and strength training can reduce trunk fat (Roubenoff et al 1999b). Exercise adds to the daily energy expenditure and this needs to be taken into account.

Lipid Disorders and Lipodystrophy
Data from the pre-HAART era show depressed total cholesterol and low density lipoprotein concentrations early in the disease with moderately increased serum triglyceride and reduced cholesterol concentrations features of advanced HIV disease (Grunfeld et al 1992). The introduction of HAART has improved life expectancy but has also seen a range of changes in body fat in
20 % - 80 % of people on HAART (Sattler 2003). Lipodystrophy is associated with atrophy of peripheral fat in the legs, arms and face and an increase in the abdominal fat, both subcutaneous and visceral, and local fat aggregations. Associated with lipodystrophy are raised serum triglyceride and cholesterol concentrations and peripheral insulin resistance with hyperinsulinaemia, hyperglycaemia and diabetes mellitus.

The pathogenesis is as yet unknown and is probably multifactorial, with HIV infection, antiretroviral drugs and host genetic factors implicated. The possible causal relationship of protease inhibitors and lipodystrophy is not confirmed because patients not on these drugs may also develop lipodystrophy, but fat wasting is faster in those on protease inhibitors (Sattler 2003). Cross sectional studies have also linked non reverse transcriptase inhibitors to lipodystrophy, on the basis of possibly causing mutations in the mtDNA gene and impairing oxidative phosphorylation (Christeff et al 2002).

Endocrine changes have also been suggested as a factor in lipodystrophy. Serum cortisol concentrations are raised in HIV+ individuals irrespective of treatment. Dehydroepiandrosterone (DHEA) concentration is normal early in the disease but then falls as the disease progresses to AIDS. The effect of this is to raise the cortisol:DHEA ratio. With HAART, those who get lipodystrophy have a marked reduction in DHEA, while HAART elevates DHEA and restores the cortisol:DHEA ratio in those who do not have lipodystrophy (Christeff et al 1999, Christeff et al 2000). In women, significantly increased testosterone concentrations and an increased FSH:LH ratio is found in lipodystrophy (Hadigan et al 2000).

Lipodystrophy has also been shown to have both physical and psychological effects ranging from bodily discomfort to low self esteem and depression. It is also seen as a visible marker of HIV disease (Power et al 2003).

Until suitable pharmacological interventions are available it is suggested that the cornerstone of management for central fat accumulation should be diet and exercise (Borderi et al 2001, Sattler 2003). Aerobic exercise on its own, (Thoni et al 2002) or in combination with a moderate fat, low glycaemic index, high fibre diet, (Roubenoff et al 2002b) or with resistance training (Jones et al 2001) has led to improvements in total abdominal fat and blood lipid profiles. Progressive resistance exercise can also decrease truncal fat as measured by DEXA and CT with little effect on limb fat distribution (Roubenoff et al 1999b).

Osteopenia and Osteoporosis
Bone metabolism is altered in HIV infection irrespective of the treatment. The prevalence of osteopenia (t score < 1 - 2.5 SD) is reported to be between 22 % and 42 % in patients on combination antiretroviral therapy (Carr et al 2001, Tebas et al 2000). Osteopenia has been linked to raised lactate concentrations (Carr et al 2001). HAART has been shown to significantly reduce both total and regional bone mineral content when compared to those not on HAART and these effects increase with the duration of HAART (McDermott et al 2001). It is suggested that HIV+ patients with osteopenia or osteoporosis should be treated similarly to HIV seronegative patients with appropriate use of nutritional supplements (calcium and vitamin D) and exercise. Hormone replacement and antiresorptive therapies might also be indicated (Mondy and Tebas 2003). The potential role of exercise in the management of osteopenia in the HIV+ is not yet clear as a 16 week programme of aerobic and resistance exercise did not alter bone mineral content in a group of HIV+ men with lipodystrophy (Roubenoff et al 1999b).

Psychological Factors

Other Factors
The potential benefits of exercise in the HIV+ population appear to outweigh the risks. Participation in regular exercise is not widely practised in many countries and it is influenced by cultural and societal norms and practices. It is interesting to note that in the USA, approximately 40 % to 60 % of HIV+ individuals report using aerobic exercise or increasing their physical exercise as an alternative form of treatment, while only about 15 % of the general population exercise on a regular basis (Roubenoff 2000). In many countries the poorer communities are most affected and adequate nutrition, suitable facilities, supervision and support for exercise may not be available or are unaffordable. Unfortunately the value of exercise has not been fully appreciated by all health professionals and some still advise their patients against exercise.

Patients too may avoid exercise as the disease makes them feel unwell. The associated diarrhoea, anorexia, nausea, secondary infection and depression are all factors that would support exercise avoidance.

Cardiopulmonary Evaluation
Should the HIV+ patient undergo a cardiac evaluation before starting exercise? Approximately 50 % of individuals who are asymptomatic of cardiac disease will have a demonstrable abnormality on ECG, echocardiogram or Doppler ultrasonography. In addition 10 % of those on HAART who are asymptomatic of heart disease will have evidence of a silent myocardial infarct on stress ECG. Duong et al. have suggested that “exercise testing might be recommended for patients with HIV who have central fat accumulation and hypercholesterolaemia” (Duong et al 2002). On the basis of the link between HIV related myocarditis and ventricular ectopic beats, those with arrhythmias and those...
with known cardiac symptoms should also be assessed before embarking on an exercise programme.

Stringer suggests that cardiopulmonary exercise testing should be routinely performed on all HIV+ patients before starting an exercise programme. The proposed benefits being the unmasking of subtle cardiopulmonary pathology and guiding exercise prescription (Stringer 2000).

Guidelines for Exercise

The use of exercise in a viral infection seems anomalous when based on the principle of avoiding exercise in the presence of a viral infection because of the risk of developing a myocarditis. To date there are no data on the long term effects of exercise on the development or progression of HIV myocarditis. Certainly in the pre HAART era, the benefits of exercise appeared to outweigh the risks. With HAART, and longer survival and the emerging lipid disorders, the effect of exercise on HIV myocarditis needs further investigation.

While there is as yet no evidence to suggest that exercise might increase a patient’s life-span, there is sufficient evidence to support the advice that HIV+ patients should be encouraged to undertake regular exercise. They will experience a training effect dependent on the normal parameters of frequency, intensity, duration, and mode of exercise. It appears that the first bout of exercise will not detrimentally affect their immune status (Roubenoff et al 1999a). Exercise should be tailored to meet their individual requirements. These may vary from aerobic training to improve work capacity or reduce abdominal lipid accumulation, to resistance training to improve strength and maintain or gain weight. General exercise training should include mixed aerobic and resistance modes.

There is no paper that gives specific guidelines on constructing an exercise programme for these patients and it is suggested that general principles are followed. Aerobic exercise programmes should therefore consist of three to five sessions a week, of twenty minutes to an hour’s duration, at an intensity of 50 - 85% of maximum heart rate or 45 - 80% of VO₂max. The patient’s symptoms, such as nausea, vomiting, diarrhoea, if present may dictate the intensity and or duration of each exercise bout. It is suggested that large muscle groups should be targeted in resistance exercise with 8 - 12 repetitions per exercise, increasing the resistance with time as the patient regains strength (Ciccolo et al 2004).

The addition of androgenic agents to resistance training appears to be an acceptable option in selected patients with AIDS wasting syndrome, or in those patients who have difficulty in complying with the training programme and who are losing weight. While regular exercise will impart psychological benefits, the benefit to their immune system is still controversial. Regular exercise is not associated with an increased risk of minor or opportunistic infection. The weight of evidence suggests that moderate exercise will not depress immunity, but may at best slow its insidious decline.

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