

Effects of Different Types of Exercise on Body Composition and Fat Distribution in HIV-Infected Patients: A Brief Review

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Abstract/Résumé

HIV infection and its treatment is associated with unfavourable metabolic and morphological abnormalities. These metabolic abnormalities, particularly alterations in body composition and fat distribution, may increase the risk for cardiovascular and metabolic complications, as well as reduce functional independence and lower self-esteem. Thus there is an urgent need to develop interventions intended to manage secondary side effects of HIV or antiretroviral therapy-related complications. In poly-treated patients, nonpharmacological interventions are a logical first step. Exercise training in particular may help alleviate some of the metabolic adverse effects associated with antiretroviral therapy by favourably altering body composition and patterns of body fat distribution. Studies have shown that exercise training, particularly aerobic training, can help reduce total body and visceral fat, as well as normalizing lipid profiles in HIV-infected patients. The results for resistance

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training, however, are less conclusive. Knowledge of the use of resistance and aerobic training and its attendant effects on insulin resistance and adipocytokines may represent an effective nonpharmacologic means for treating metabolic complications of HIV-infected persons who are receiving appropriate antiretroviral therapy. In this brief review we examine the effects of aerobic and resistance training on body composition, body fat distribution, and selected metabolic outcomes.

On associe l'infection à VIH et à son traitement à des anomalies métaboliques et morphologiques désavantageuses. Ces anomalies métaboliques, en particulier les altérations de la composition corporelle et la répartition des graisses, augmentent le risque de complications métaboliques et cardiovasculaires et entraînent une diminution de l'autonomie fonctionnelle et de l'estime de soi. Il est impératif d'élaborer des plans d'intervention afin d'atténuer les effets secondaires du VIH et des complications associées au traitement antirétroviral. Chez les patients sous thérapie multiple, les interventions non pharmacologiques constituent la première étape. L'entraînement physique contribue à l'amélioration de certains effets secondaires métaboliques associés au traitement antirétroviral en modifiant favorablement la composition corporelle et la répartition des graisses. D'après de nombreuses études, l'entraînement physique, et surtout l'entraînement aérobic, s'avère efficace dans la réduction des graisses corporelles et viscérales et dans la normalisation du profil lipidique des patients infectés au VIH. Les observations concernant l'entraînement à la force sont moins concluantes. Une meilleure connaissance de l'entraînement aérobic et de l'entraînement à la force et de ses effets sur l'insulinorésistance et sur les adipocytokines devrait permettre de constituer un traitement non pharmacologique efficace des complications associées à la thérapie antirétroviral chez les patients infectés au VIH. Dans ce court article-synthèse nous analysons les effets de l'entraînement aérobic et de l'entraînement à la force sur la composition corporelle, la répartition des graisses, et sur certaines adaptations métaboliques.

Introduction

The introduction of highly active anti-retroviral therapy (HAART) in the 1990s has dramatically reduced the incidence of opportunistic infections and decreased the mortality and morbidity associated with HIV infection. HAART has reduced AIDS-related mortality in HIV-infected patients by inducing favourable virological control and by increasing immunological response (CD4 lymphocyte count) and clinical effects (reducing the incidence of opportunistic infection, length of hospitalization). With the current available antiretrovirals, an optimal virological control could be obtained in most HIV-infected patients. Antiretroviral therapy is usually followed by progressive improvements on the infected person's immune status (Pallela, 1998; Portsmouth et al., 2003).

Despite significant benefits associated with HAART, HIV infection and its therapy has been associated with the development of several metabolic complications. These include: increased central adiposity, peripheral lipotrophy, peripheral insulin resistance, diabetes, dyslipidaemia and hypertriglyceridemia, osteoporosis and osteopenia (Carr et al., 1998; Martinez et al., 2001; Safrin and Grunfeld, 1999). These complications may predispose patients to premature risk of metabolic and cardiovascular diseases. For example, several studies have shown premature atherosclerosis (Flynn and Bricker, 1999; Henry et al., 1998) and an in-

crease in cardiovascular mortality in HIV-infected patients (Mary-Krause et al., 2001). Therefore HIV-infected patients undergoing antiretroviral therapy for extended periods of time may be at increased risk for metabolic and cardiovascular complications (Barbaro, 2003).

Issues of Fat Redistribution

One important complication associated with HAART is the lipodystrophy syndrome, which may complicate the treatment of HIV-related problems. The general features of this complex syndrome include loss of fat, frequently observed in the face, arms, and legs (subcutaneous lipoatrophy); the accretion of adipose tissue in the abdomen **and dorsocervical spine** (lipohypertrophy); and sporadic lipomas. The etiology of the lipodystrophy, however, remains enigmatic. Earlier works supported an association between problems of fat redistribution with the use of protease inhibitors (Carr et al., 1998). However, subsequent studies also showed similar problems with non-nucleoside reverse transcriptase inhibitors (Lo et al., 1998). Still other researchers suggest that the duration of HIV infection, CD4 cell count nadir, and sex and race may play contributing roles. Although the antiretroviral drugs may be considered a major risk factor in the development of lipodystrophy, further research is needed in order to identify which antiretroviral regimen may aggravate problems of lipodystrophy development.

Presently the management of lipodystrophy has been problematic, and to date there have been no clinically proven therapies (Currier, 2000). It is well established, however, that exercise training may be effective in reducing obesity related abnormalities such as those observed in the metabolic syndrome. Partial evidence for this assertion is that exercise training on body fat and central fat has been extensively studied in individuals who are not HIV-infected. The general consensus is that when total volume of exercise is high enough and prolonged over an extended period of time, reductions in total and central body fat are observed which coincides with improvements in body composition (Ross et al., 2000). These findings have raised the possibility that exercise training may be a valuable nonpharmacological intervention for treating lipodystrophic disorders in HIV-infected patients.

Thus, increased attention has been directed toward exercise training as a beneficial lifestyle addition in the treatment regimen of HIV-positive individuals. It is possible that exercise training may contribute to an amelioration of certain metabolic adverse effects associated with antiretroviral therapy by favourably altering patterns of body fat distribution. In addition, it has been shown that exercise training in HIV-infected individuals is safe and does not significantly increase circulating HIV RNA or decrease CD4 counts (Smith et al., 2001; Stringer et al., 1998). Thus the purpose of this review is to evaluate the reported role of exercise training on metabolic and body composition factors associated with lipodystrophy in HIV-infected individuals. We will consider the role of aerobic and resistance training and their potential effects on body composition and body fat distribution in HIV-infected individuals. These studies and their principal conclusions are summarized in Table 1. Greater detail in the discussion of these studies is provided in the following sections.

Table 1 Summary of Resistance Training, Aerobic Training, and Diet Studies

Reference	Objective	Design	Population	Methods	Major Findings
Yarasheski et al. (2002)	Examine the effects of RT on metabolic complications	16 weeks RT, 4 × week for 1–1.5 hr/day	18 HIV patients No control	DXA	RT promoted clearance of triglycerides in the circulation
Roubenoff et al. (1999a)	Assess the efficacy of PRT in increasing strength and LMB in HIV-infected adults	Highly PRT 8 wks + 8-wk follow-up of free physical activity	25 adults: 20 men and 5 women	Self-selected diet, DXA	PRT significantly increased LBM and strength, decline in fat
Roubenoff and Wilson (2001)	Improve functional status in HIV ⁺ wasted and not wasted	8 wks, 3 × week followed by 8 wks usual phys activity	6 Pts w/wasting; 19 with HIV without wasting	DXA	Increased functional status by increasing strength and LMB
Roubenoff et al. (2002)	Effects of diet and RT and AT on lipodystrophy	4 months of AT and RT 3 × week; Fat glycemic diet	Case study with HIV; No control	DXA, CT	Exercise and diet can reverse several aspects of lipodystrophy
Agin et al. (2001)	Effects of PRT, PRO, PRT-PRO on BCM, MS, QOL	14 wks randomized, PRT, PRO, combined, 6 wks control period	30 HIV women	TBK DXA, MRI, QOL	PRT increased BCM, MM, QOL; PRT-PRO did not increase BCM more than PRT alone
Smith et al. (2001)	Effects of AT on weight and body composition	12 week AT, 3 × week for 30 min	60 HIV randomized	Anthropometric measurements exper. control	AT decreased fatigue, weight, BMI, SAT, and central fat

Thoni et al. (2002)	Effect of AT on body composition and metabolic disorders	4 months of aerobic training	17 HIV patients No control	CT scan	AT reduced visceral fat and lipid disorders
Stringer et al. (1998)	Exercise improves aerobic fitness, immunological indices, quality of life	6 weeks of aerobic exercise training	34 randomized: control, moderate, heavy	Gas exchange lactic acidosis threshold	Exercise and diet can reverse several aspects of lipodystrophy
Gavrila et al. (2003)	Relationship among habitual exercise, diet, and metabolic abnormalities	Cross-sectional	120 participants	DXA, CT Diet	Exercise and vitamin E independently and negatively HIV metabolic syndrome
Roubenoff et al. (1999b)	Examine if RT and a component of AT reduces trunk fat	16 weeks, 3 × wk + 20 min AT and 1 hr RT	10 men with HIV No control	DXA	Exercise training significantly reduced trunk fat by 14%
Jones et al. (2001)	ET improves body lipids profile while attenuating the adverse body compositional changes	10 wks, 3 × wk combined aerobic and resistance training	5 men and 1 woman with fat wasting	Not listed	Enhanced functional capacity, reduced SAT TC, triglycerides, and increased body mass

Note: ET: exercise training, AT: aerobic training, RT: resistance training PRT: progressive resistance training CT: computed tomography, DXA: dual x-ray absorptiometry, MRI: magnetic resonance imaging, LMB: lean body mass, BMI: body mass index, BCM: body mass index, TBK: total body potassium-40, PRO: protein group, PRT-PRO: combined progressive resistance and protein group, MS: muscle strength, MM: muscle mass, QOL: quality of life, SAT: subcutaneous adipose tissue, TC: total cholesterol.

RESISTANCE TRAINING

Resistance training offers the possibility of increasing fat-free mass and reducing fat mass, but its effects on central body fat are controversial. Yarasheski et al. (2001) examined the effects of 64 sessions of resistance training on body composition and plasma lipids in 18 asymptomatic HIV-infected male volunteers. Body composition was measured with dual energy x-ray absorptiometry (DXA), and thigh muscle area with axial proton-magnetic resonance imaging. None of these subjects, however, were categorized as lipodystrophic.

All 18 volunteers were on HAART. Whole-body lean and trunk adipose mass increased by 2.5% (1.4 kg) and 2.6% (0.2 kg), respectively, but there was no change in whole-body adipose mass. Measures of thigh muscle cross-sectional area increased by 7.3%. Yarasheski et al. (2001) also noted a significant decrease in fasting triglycerides, but no changes in total cholesterol, HDL-cholesterol, LDL-cholesterol, or fasting insulin. They noted that the decrease in triglyceride levels was greatest in subjects with the highest baseline triglyceride levels. Interestingly, they noted a trend in which the increase in fat-free mass was associated with a decline in fasting triglycerides, suggesting that this tissue may be responsible for increased clearance of triglycerides. This study suggests that progressive resistance training may be an effective lifestyle intervention to prevent AIDS-related wasting.

In another study, Roubenoff et al. (1999a) showed that individuals who participated in an 8-week resistance training program showed a significant increase in fat-free mass (FFM) and a decrease in fat mass (FM), as measured by DXA. This increase in FFM was maintained even after 8 weeks of self-selected activity; however, there was a regain in FM (1 kg). An interesting subanalysis revealed that 6 patients with AIDS-related wasting had a slightly higher gain in FFM and FM. Roubenoff et al. (1999a) suggested that progressive resistance training is an effective intervention for enhancing FFM and potentially decreasing fat mass in individuals suffering from the effects of AIDS wasting.

AIDS-related wasting is associated with a decline in physical functioning. A relevant question is whether the reported changes in body composition and body fat distribution translate into improved physical function. Roubenoff and Wilson (2001) examined the effects of 8 weeks of resistance training in wasted and nonwasted patients on a validated physical function scale and body composition. Body fat distribution was not evaluated in their study. Interestingly, wasted and nonwasted patients did not differ at baseline with respect to physical function scores. The resistance training program increased physical functioning in the wasted patients but not in the nonwasted patients. Roubenoff and Wilson found that the increase in fat-free mass and change in muscular strength were two independent predictors of the increase in physical function. These results confirm and extend the previous studies of resistance training in that improvements in strength and fat-free mass translate into favourable changes in physical functioning.

RESISTANCE TRAINING AND DIET

Several studies have examined the combined effects of resistance training and a dietary intervention on metabolic outcomes. For example, in a case report study, Roubenoff et al. (2002) examined the effects of 4 months of resistance training

and a moderate-fat/ low glycemic index/ high fiber diet on several aspects of lipodystrophy. The patient was a 44-year-old Caucasian man who was treated with antiretroviral triple therapy. The most remarkable finding was the reduction in visceral fat as measured by computed tomography: a 52% decrease in visceral fat and a 43% decrease in total abdominal fat. Concomitant with these positive changes in central fat indicators, favourable changes were noted in the lipid profile. Roubenoff et al.'s study showed that diet and exercise therapy can reverse some of the metabolic changes associated with lipodystrophy.

Agin et al. (2001) examined the singular and combined effects of whey protein and resistance training on body cell mass and quality of life in women with HIV who were classified as wasted. Theirs was one of the few studies performed exclusively on women. They tested the hypothesis that an additional supplement of whey protein may augment the increases in body cell mass. Contrary to their hypothesis, whey protein and resistance exercise did *not* augment the increase in body cell mass vs. resistance training alone. Thus Agin et al.'s results do not favour the notion that combined protein supplementation with resistance training augments body cell mass in wasted patients. Similar to other studies, quality-of-life indicators improved after a 14-week exercise program. Despite the absence of an effect of the protein supplementation, it should be noted that resistance training increased muscular strength, body cell mass, and quality of life.

AEROBIC TRAINING

Aerobic training offers the potential advantages of increasing cardiovascular fitness and high levels of energy expenditure that may have a favourable impact on reducing body fatness. Smith et al. (2001) examined the effects of aerobic training only on body weight, body composition, and general fatigue. Sixty volunteers were randomized either to a 12-week aerobic training program or a control condition (usual physical activity). The aerobic training program consisted of 3 days of exercise per week at 60 to 80% of $\dot{V}O_2$ max. Body composition was estimated from subcutaneous skinfolds, and body fat distribution from circumference. Smith et al. observed that body weight decreased by approximately 1 kg. The change in body weight was also accompanied by reductions in skinfolds (i.e., a proxy measure of subcutaneous body fat) and a reduction in waist circumference (a proxy measure of central body fat). As expected, aerobic fitness increased and measures of fatigue decreased. No changes were noted in CD4 cell count or viral load. These results suggest that aerobic training of moderate duration is effective in reducing subcutaneous and central body fat, as well as enhancing quality of life by decreasing measures of fatigue.

Thoni et al. (2002) examined the effects of 4 months of aerobic training in lipodystrophic and dyslipidemic adults. Abdominal adipose tissue, visceral adipose tissue, and subcutaneous adipose tissue were determined by computed tomography. Thoni et al. noted a mean reduction of 12 cm² in visceral fat after training, whereas subcutaneous abdominal adipose tissue did not change significantly. No changes were noted in body composition as measured from DXA. Concomitant with the changes in visceral fat, aerobic training reduced total cholesterol and fasting triglycerides, and increased HDL-cholesterol, but no changes were noted

in LDL-cholesterol or insulin resistance as estimated by the HOMA index. The decline in visceral fat was related to improvements in the lipid profile. Thoni et al.'s results support the fact that moderate aerobic training reduces central adiposity, and these favourable changes led to a reduction in cardiovascular risk factors in the HIV patients.

Stringer et al. (1998) studied the effects of 6 weeks of aerobic training on aerobic fitness and quality of life in HIV patients. They examined two levels of exercise, moderate and heavy intensity, on quality-of-life indicators. In all, 77% of the patients completed the study. All but two were on antiretroviral therapy. The more intense exercisers, as expected, had a greater % increase in $\dot{V}O_{2\max}$ than the moderate exercisers and the control group. No changes were noted in immune function. Quality-of-life indicators improved in both the moderate and intense exercise groups, but there were no differences between groups. This study basically documents the fact that moderate and heavy exercise is a safe intervention for HIV patients and can markedly improve quality-of-life indicators.

In a cross-sectional study, Gavrilu et al. (2003) examined the interrelationships among habitual exercise levels and the presence of metabolic abnormalities using bivariate and multivariate regression analyses in 120 subjects. Diet was evaluated using a food frequency questionnaire which allowed Gavrilu et al. to estimate the level of energy, macro- and micronutrients, and food-group consumption. The exercise questionnaire evaluated the intensity, type, frequency, and duration of exercise. Metabolic measurements included fasting serum glucose, insulin and lipid levels, as well as insulin resistance. Visceral adipose tissue and subcutaneous adipose tissue were measured using computer tomography scan. Fasting triglyceride levels were negatively associated with total exercise index.

No relationship was found between total or aerobic exercise and fasting LDL, HDL, and total cholesterol in the entire group or in any of the fat redistribution subgroups. Interestingly, vitamin E intake was inversely associated with lower diastolic blood pressure in HIV-positive subjects. These cross-sectional results preclude conclusions regarding causality, but suggest that the higher exercise levels are associated with reduced manifestations of the metabolic syndrome in HIV patients.

COMBINED RESISTANCE AND AEROBIC TRAINING

Two studies have investigated the effects of combined resistance and aerobic training on body composition in HIV-infected patients. Roubenoff et al. (1999b), in an open-labeled pilot study, examined the effects of resistance training performed for 16 weeks, 3 times per week with an aerobic component: 20 minutes on treadmill or stationary bicycle. Fourteen men with an increased abdominal girth enrolled in the study and 10 completed it. At the end of 16 weeks of exercise, there was a significant decline in total body fat by 10% as well as a 13% decline in trunk fat, whereas lean body mass slightly increased. Roubenoff et al. concluded that a combined aerobic and resistance training program could reduce central body fat redistribution in HIV-infected patients.

In the second study, Jones et al. (2001) exposed 6 HIV-positive individuals with established lipodystrophy to 10 weeks of combined aerobic and resistance

training. Several changes are noteworthy. First, body mass increased by 5.5% due to an increase in FFM and decline in FM. The method for measuring body composition, however, was not specified. In addition, Jones et al. noted a 4.7% decrease in waist-to-hip ratio, a proxy measure of central body fat distribution. These results suggest that combined aerobic and resistance training resulted in positive changes in body composition and a reduction in central fat deposition. In addition, arm and leg circumferences increased by 9% and 8%, respectively. These results suggest that exercise training may be useful for offsetting AIDS-related wasting. Additional positive changes in this study included a 17.6% decline in total cholesterol and a 25% decline in fasting triglyceride levels. This study confirms the magnitude of changes in body composition observed by Roubenoff et al. (1999b).

Conclusions Regarding Training Effects

The four studies (Agin et al., 2001; Roubenoff et al., 1999a; Roubenoff and Wilson 2001; Yarasheski et al., 2001) that examined the effects of the resistance training on body fat remain inconclusive (Table 2). One study showed that body fat decreased by 9% (Agin et al., 2001), whereas two studies showed no change in body fat (Roubenoff et al., 1999a; Yarasheski et al., 2001). However, another study observed a 12% increase in body fat in wasted patients and an 8% decrease in nonwasted patients (Roubenoff and Wilson, 2001). Based on these studies, it is difficult to conclude the directionality of changes in body fat with resistance training and its influences on fat mass in HIV-infected patients. However, in the study of Roubenoff and Wilson (2001), the enhancing effect of body fat in wasted patients suggests that exercise may be perceived as improving the precision of energy balance regulation around a given body weight set point.

The effects of aerobic training on body fatness, however, are somewhat more conclusive. Two studies reported results of the effects of aerobic training on body fat (Smith et al., 2001; Thoni et al., 2002) (Table 3). For example, Smith et al. (2001) showed a decrease in skinfolds in HIV-infected patients who enrolled prior

Table 2 Changes in Total Body and Trunk Fat After Resistance Training

Reference	Method	Variables	% Change
Yarasheski et al. (2001)	DXA	Body fat	0%
		Trunk fat	2.6%
Roubenoff et al. (2002)	DXA	Body fat	0%
Roubenoff et al. (1999a)	DXA	Body fat (wasted group)	12%
		Body fat (nonwasted group)	-8%
Agin et al. (2001)	DXA	Body fat	-9%

Note: DXA = dual energy x-ray absorptiometry.

Table 3 Changes in Total Body and Visceral Fat After Aerobic Training

Reference	Method	Variables	% Change
Smith et al. (2001)	Skinfolds	Triceps	-19%
		Central	-11%
		Peripheral	-24%
Thoni et al. (2002)	CT	TAT	-13%
		VAT	-12%
		SAT	0%

Note: CT = computer tomography; TAT = total abdominal adipose tissue; VAT = visceral adipose tissue; SAT = subcutaneous adipose tissue.

Table 4 Changes in Body Fat and Fat Redistribution After Aerobic and Resistance Training Combined

Reference	Method	Variables	% Change
Roubenoff et al. (1999b)	DXA	Body fat	-10%
		Trunk fat	-13%
Jones et al. (2001)	Not specified	Body fat %	-14%
Roubenoff et al. (2002)*	DXA	Fat mass	-33%
	CT	Visceral fat	-52%
		Subcutaneous abdominal fat	-38%

Note: DXA = dual energy x-ray absorptiometry; CT = computer tomography. *Case report study using only one subject and adding a diet component in the combined aerobic and resistance training.

to the widespread use of antiretroviral therapy, suggesting a decrease in total body fatness. Thoni et al. (2002) reported a 13% reduction in total abdominal adipose tissue as well as a 12% decrease in visceral adipose tissue, and no changes in subcutaneous adipose tissue in HIV patients undergoing antiretroviral therapy. Collectively these studies show that aerobic training could be useful in reducing total fat mass and possibly visceral fat in HIV patients.

Two studies reported data on the effects of combined aerobic and resistance training on body fat in HIV-infected patients with lipodystrophy (**Jones et al.**,

2001; Roubenoff et al., 1999b) (Table 4). Roubenoff et al. (1999b) reported a reduction of 10% body fat and 13% trunk fat in HIV-infected men with lipodystrophy. A second study (Jones et al., 2001) reported a 14% decrease in body fat % after a 10-week study involving HIV-infected men and women with lipodystrophy. **Roubenoff et al. (2002)** reported that when a diet component is added to the combined aerobic and resistance training, major fat reductions are observed.

Thus, to date the available data suggest that combined aerobic and exercise is more effective in reducing body fat and increasing lean body mass in HIV-infected patients with lipodystrophy than exercise alone. Therefore, given the pattern of body fat redistribution (lipoatrophy and lipohypertrophy) in HIV-infected patients, we suggest that a combined regimen of aerobic and resistance training could be incorporated with their medications. Although peripheral fat loss is not desirable in HIV lipodystrophic patients with aerobic training, the combined effect of aerobic and resistance training may be useful in reducing fat accumulation and increasing lean body mass, which could compensate for the peripheral fat loss.

FUTURE PERSPECTIVES

With the notion that a cure for HIV infection may not come soon, the management of metabolic abnormalities associated with HIV infection and its treatment has taken on added importance. Although a straightforward, pharmacological approach is intuitively appealing, it is unlikely that a single agent will be effective in treating the complex metabolic complications due to HIV infection and its therapy. Thus it is imperative to consider the use of nonpharmacologic approaches to reduce, improve, or prevent some HIV- or antiretroviral therapy-related complications. Knowledge of the use of resistance and aerobic training and its attendant effects on insulin resistance and adipocytokines may represent an effective treatment for metabolic complications of HIV-infected persons receiving antiretroviral therapy.

We suggest the following scientific methodologies to improve our understanding of the role of exercise training on body composition in AIDS patients:

- More complete subject characterization (i.e., lipodystrophic or not) that clearly defines the type of antiretroviral regimen and the medical condition of the patient (i.e., wasted vs. nonwasted) prior to initiating the exercise program.
- Greater methodological precision in the assessment of body composition and body fat distribution with the use, for example, of dual energy x-ray absorptiometry and computed tomography.
- Rigorous experimental designs (i.e., randomized trials) that examine the effects of different exercise regimens vs. placebo conditions on major metabolic and cardiovascular outcome variables.
- Experimental designs that may attempt to verify whether early initiation of exercise in patients undergoing HAART can prevent lipodystrophy.
- The inclusion of more direct measures of insulin sensitivity (i.e., clamp methodology) to more fully examine the role of changes in body composition and body fat distribution with alterations in insulin sensitivity.

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