Aerobic Fitness, Fatigue, and Physical Disability in Systemic Lupus Erythematosus

COLIN TENCH, DAVID BENTLEY, VERONICA VLECK, IAN McCURDIE, PETER WHITE, and DAVID D'CRUZ

ABSTRACT. ***Objective.*** To measure aerobic fitness, muscle strength, fatigue, and physical disability in patients with systemic lupus erythematosus (SLE).

Methods. Ninety-three patients with SLE and 41 sedentary controls were recruited into the study. Aerobic fitness was assessed by monitoring peak and submaximal oxygen uptake, heart rate, duration of exercise, and perceived exertion during a treadmill-walking test. Strength was measured using voluntary isometric quadriceps contraction. Symptomatic measures included physical and mental fatigue, mood, sleep, and functional incapacity.

Results. Compared to sedentary controls patients with SLE had significantly reduced levels of aerobic fitness (mean VO_{2peak} SLE patients, 23.2 ml/kg/min vs controls, 29.6 ml/kg/min; $p < 0.001$) and reduced exercise capacity (mean exercise duration SLE patients, 10.4 min vs controls, 13.1 min; $p < 0.001$). The SLE patients also had reduced muscle strength (mean maximum voluntary quadriceps contraction SLE patients, 298 N vs controls, 376 N; $p = 0.003$). Resting lung function was also significantly worse in the SLE patients (mean FEV_1 SLE patients, 2.6 l vs controls, 2.9 l; $p = 0.002$). Fatigue ($p < 0.001$), depressed mood ($p < 0.001$), poor sleep quality ($p < 0.001$), and functional incapacity ($p < 0.001$) were all significantly greater in the SLE patients. Linear regression models suggested that physical disability correlated with aerobic fitness ($p < 0.001$), fatigue ($p = 0.005$), body mass index ($p = 0.01$), and depression ($p = 0.05$) and that fatigue correlated with depression ($p < 0.001$).

Conclusion. Patients with SLE were less fit with reduced exercise capacity, reduced muscle strength, more fatigue, and greater disability compared to sedentary controls. Treatments developed to manage depression and improve aerobic fitness should be considered in the overall treatment of fatigue and disability in SLE. (J Rheumatol 2002;29:474–81)

Key Indexing Terms:
FATIGUE DISABILITY AEROBIC FITNESS

Fatigue (a subjective feeling of extraordinary tiredness) is a common symptom experienced by individuals with systemic lupus erythematosus (SLE) and is associated with a diminished ability to perform everyday tasks[1]. In most cases the cause of fatigue is not known, although it is likely to result from a number of contributing factors, such as disease activity[1-4], mood disorder[1,5], poor sleep patterns[1,5], and associated fibromyalgia[6,7]. Other important contributing factors might include inferior physical conditioning and muscle strength, possibly as a result of reduced levels of physical activity. Indeed some patient information leaflets recommend frequent periods of rest to cope with the fatigue of SLE. Two small studies have examined physical deconditioning in SLE[8,9]. Robb-Nicholson, *et al* showed that compared to published age and sex matched norms, patients with SLE performed at 45% of their expected maximal aerobic capacity (VO_{2max}) and fatigue, measured using a visual analog scale, was inversely correlated with the duration of the exercise test, although not with VO_{2max} itself[8]. A study by Daltroy, *et al* measured exercise duration during a graded exercise test in 34 patients with SLE and concluded that the patients were deconditioned compared to published age and sex matched norms[9]. However, both studies were limited by the small number of patients involved, the use of published normative data, and the insensitivity of the fatigue measure.

Our aim was to compare physiological measures, including peak aerobic capacity (VO_{2peak}) and muscle strength and symptomatic measures, including fatigue, sleep, and functional incapacity between patients with SLE and healthy sedentary controls. We describe baseline infor-

From the Bone and Joint Research Unit and the Department of Psychological Medicine, St. Bartholomew's, the Royal London School of Medicine and Dentistry and the National Sports Medicine Institute, London, UK.

C.M. Tench was funded by the Arthritis Research Campaign (TO519), Special Trustees of St. Bartholomew's Hospital (XMKY), and the British Medical Association Doris Hillier Award.

C.M. Tench, MB, BChir, Specialist Registrar in Rheumatology, St. Bartholomew's; D.J. Bentley, MSc, Exercise Physiologist; V.E. Vleck, MSc, Exercise Physiologist, National Sports Medicine Institute; I. McCurdie, MBBS, Senior Registrar in Rheumatology, Bone and Joint Research Unit; P.D. White, MD, Senior Lecturer and Honorary Consultant Psychiatrist, Department of Psychological Medicine, St. Bartholomew's; D.P. D'Cruz, MD, Senior Lecturer Honorary Consultant Rheumatologist, Bone and Joint Research Unit and the Royal London School of Medicine and Dentistry.

Address reprint requests to Dr. C.M. Tench, Rheumatology Department, Ground floor East Wing, Charing Cross Hospital, Fulham Palace Road, London, W6 8RF, United Kingdom. E-mail: Colin.Tench3@which.net

Submitted March 9, 2001; revision accepted September 11, 2001.

mation of patients who had agreed to participate in a prospective, randomized, controlled trial of exercise therapy as a potential treatment for fatigue in SLE.

MATERIALS AND METHODS

Study participants. Ninety-three female patients fulfilling the American College of Rheumatology revised criteria for SLE[10,11] were recruited through a connective tissue disease clinic at St. Bartholomew's and The London NHS Trust. The study involved an incremental exercise test to exhaustion and therefore patients were excluded if they had severe myositis, active nephritis, active neurological disease, or active, severe cardiac or pulmonary disease. Pregnant patients and patients under 16 years or over 55 years were also excluded. Patients with a previous history of myocardial infarction or ischemic heart disease, a diastolic blood pressure > 100 mm Hg, severe arthritis in 3 or more weight bearing joints or serum creatinine > 265 mmol/l were also excluded. All patients had been on stable therapy for the previous 2 months (Table 1). Thirty-one eligible patients declined to participate in the study.

Forty-one healthy but sedentary female controls were recruited by personal referral and an E-mail request for staff volunteers at St. Bartholomew's and The Royal London School of Medicine and Dentistry. Thirty-seven of these volunteers exercised less than once a week and 4 volunteers exercised once a week on average.

Ethical approval was obtained from the district research ethics committee and all subjects gave valid and informed consent before entering the study.

Symptomatic measures. All questionnaires were completed by subjects immediately before the physiological assessments. Fatigue was measured with the Fatigue Severity Score (FSS)[12], the Chalder Fatigue Scale (CFS)[13], and a visual analog scale (VAS)[14]. The FSS is a 9 item questionnaire, each item being scored from 1 to 7 and an overall score computed in a range of 1 to 7. The CFS is a 14 item questionnaire, each item being scored from 0 to 3, generating a score between 0 and 42. The scale yields high internal consistency with the Cronbach alpha score for the total fatigue scale ranging from 0.88 to 0.99 calculated for all items[13]. The validity of the scale has been confirmed by comparison with the fatigue items of the Revised Clinical Interview Schedule[15] and the scale has been shown to have good convergent validity and reasonable discriminant validity as an estimator of change evaluated in an open treatment trial[16]. The VAS is composed of 4 separate scales measuring pervasive physical fatigue, pervasive mental fatigue, postexertional physical fatigue, and postexertional mental fatigue. Each scale is scored between 0 (extremely energetic) and 100 (extremely tired) so that the scale is normally distributed[14]. The scores of the 4 scales were combined to give a composite fatigue score (maximum 400), which has been shown to measure change in fatigue in a trial of exercise therapy in patients with chronic fatigue syndrome[17]. In all 3 questionnaires a higher score indicates increased severity of fatigue. All 3 fatigue questionnaires correlate highly with each other[1].

Quality of sleep was assessed using the Pittsburgh Sleep Quality Index[18]. This is a self-rated questionnaire comprising 19 different items, generating an overall score between 0 and 21, with a higher score indicating worsening sleep quality. Functional incapacity was measured using the Medical Outcomes Study Short Form Health Survey (SF-36)[19]. This is a 36 item questionnaire generating component scores for physical function, physical role, bodily pain, general health, vitality, social function, emotional role, and mental health. Each component score is between 0 and 100, a higher score indicating better function. Anxious and depressed mood were assessed using the Hospital Anxiety and Depression scale (HAD)[20], which was designed to assess mood in patients with physical disease. It is a 14 item questionnaire generating a separate score for anxiety and depression between 0 and 21, a higher score indicating increasing severity of depression or anxiety. A HAD score of 8 or above suggests possible mood disorder and 10 or above suggests the presence of a pathological mood disorder. Disease activity in the SLE patients was measured using the Systemic Lupus Activity Measure (SLAM)[21]. SLAM was chosen because it has been shown to be the global disease activity score most sensitive to change over time and the patients were going to participate in a trial of graded exercise therapy[22]. Disease damage was measured using the Systemic Lupus International Collaborating Clinics (SLICC)/ACR Damage Index[23]. The SLE patients were bled at the time of their assessment and blood variables needed to score the SLAM were measured.

Table 1. Medication taken by the patients with SLE.

Medication	No. of Patients (n = 93) (%)
Prednisolone ≤ 7.5 mg	29 (31)
Prednisolone > 7.5 mg	6 (7)
Hydroxychloroquine	53 (57) 200 mg or 400 mg
Azathioprine	21 (23) 100 mg or 150 mg
Antidepressants	13 (14)
β-blockers	3 (3)

Physiological assessments. Skinfold measurements were taken at 4 separate sites (triceps, biceps, subscapular, and supraspinal) using skinfold calipers to give a total score in millimeters as an indication of body composition[24]. Body mass and height were measured so that the body mass index (BMI) could be calculated. The circumference at the level of the umbilicus (waist) and at the greatest protrusion of the gluteals (hip) was also measured in order to calculate the waist-hip ratio. Forced vital capacity (FVC) and forced expired volume in 1 second (FEV_1) were measured with a vitalograph spirometer. Predicted values were calculated using a standard formula adjusted for ethnicity[25]. Maximum voluntary isometric force of the quadriceps muscle of the dominant leg was measured. Subjects were seated in a specially adapted rigid, straight-backed chair and asked to push against a strap attached just proximal to the ankle joint and connected to a force transducer. Subjects were instructed to exert as maximally as possible for 5 seconds following an auditory count and the best of 5 repetitions was recorded. VO_{2peak} was measured during a walking test carried out on a motor driven treadmill. Speed was held constant at 5 kph with gradient increases of 2.5% occurring every 2 minutes except the first increment, which was from 0 to 5%. A number of the SLE patients were unable to walk at 5 kph and for these individuals the treadmill speed was reduced to a speed they could manage, between 1 and 4 kph. The gradient increments were the same and once the test was started the treadmill speed remained constant. Expired gases were analyzed continuously for ventilatory equivalents of oxygen, carbon dioxide, and minute ventilation by a breath by breath system (MedGraphics CardiO_2 and CPX/D systems using Breeze2 software) calibrated prior to each test. Heart rate was monitored continuously using a 3 lead ECG. Ratings of perceived exertion (RPE) were recorded with the Borg 20 point scale in the last 30 seconds of each treadmill stage[26]. Subjects were encouraged to continue the exercise test to maximum exertion; however, the test was terminated at volitional exhaustion. Peak levels of all variables and the test duration were recorded at this point. The peak respiratory exchange ratio was also recorded. This represents the amount of carbon dioxide produced divided by the amount of oxygen consumed and a respiratory exchange ratio exceeding 1.0 to 1.2 indicates the subject is giving maximum effort[27]. The recovery heart rate 3 minutes after the test finished was also recorded. Age-predicted maximum heart rate was calculated from the formula 210 – (age × 0.65)[28] and the maximum heart rate achieved was expressed as a percentage of this.

The submaximal RPE, heart rate, and VO_2 measurements in the SLE patients who were unable to perform the treadmill test at 5 kph were adjusted to reflect that less work was needed to perform the test at a slower speed. Using a standard formula[29] the power value per kilogram of body weight at each 2 minute stage was calculated for different treadmill speeds. Hence the submaximal RPE, heart rate, and oxygen uptake measurements at different treadmill speeds could be directly compared at different power levels rather than according to time on the treadmill.

Since the SLE patients were about to be entered into a therapeutic trial it was not possible to assess them blindly; however, care was taken to ensure that the same explanation and encouragement was given to all subjects.

Statistical analysis. Statistical analysis used the SPSS 10.0 for Windows software package. The distribution of the data was assessed using a normal probability plot and K-S Lilliefors tests for normality. Student t tests or Mann-Whitney tests were used to compare means and medians of each variable in the 2 groups as appropriate. All p values are 2 tailed. Chi-square analysis with Fisher's exact test for small numbers was used for categorical data. We compared the submaximal responses to exercise between the 2 groups by comparing the area under the curve of between 0.68 and 1.7 watts/kg inclusively, corresponding to between 4 and 10 minutes on the treadmill at 5 kph, using Student t test. Forward stepwise linear regression models were calculated on the SLE patients to explore the relationship between the dependent variable of physical disability measured using the physical function scale of the SF-36 questionnaire and the independent variables of fatigue, mood, sleep, BMI, aerobic fitness, isometric strength, and lung function. Similar models were calculated using exercise test duration as the dependent variable as an objective measure of physical disability. Only the SLE patients who were able to do the test at 5 kph were included in this model. Also, forward stepwise linear regression models were calculated to explore the relation between the dependent variable of fatigue and the independent variables of mood, sleep, disease activity with fatigue component removed, BMI, isometric strength, lung function, and VO_{2peak}.

RESULTS

There were no significant differences between the groups in age, height, BMI, skinfold thickness, waist/hip ratio, ethnic origin, or the proportion of smokers. However, the SLE patients did have a significantly higher body mass than the controls and were more likely to be unemployed (Table 2). In the SLE group, the median (interquartile range) disease duration was 30 months (10–84), the median SLAM score was 5 (3–8), and the median SLICC/ACR Damage Index score was 0 (0–0). These patients thus had mild, relatively early disease with negligible organ damage.

Physiological measures. There were 69/93 (74%) SLE patients who were able to do the exercise test at a treadmill speed of 5 kph, 11/93 (12%) at 4 kph, 10/93 (11%) at 3 kph, 2/93 (2%) at 2 kph, and 1/93 (1%) at 1 kph. All the control patients did the exercise test at a treadmill speed of 5 kph. There were significant differences between the groups in all the physiological measures except recovery heart rate (Table 3). Compared to the healthy sedentary controls the SLE patients had significantly shorter test duration, lower VO_{2peak}, lower maximum minute ventilation, and lower respiratory exchange ratio, and terminated the test at a significantly lower maximum heart rate. There were 31/93 (33%) SLE patients who had a peak respiratory exchange ratio < 1.1 compared to 5/41 (12%) controls (chi-square 6.5, p = 0.01). The maximum voluntary quadriceps contraction was also significantly reduced in the SLE patients compared to controls.

Resting lung function measures were significantly reduced in the lupus patients. There were 15/93 (16%) SLE patients who had FEV_1 less than 75% of predicted and 18/93 (19%) SLE patients who had FVC less than 75% of predicted. One control patient had FEV_1 and FVC less than 75% of predicted.

Perceived exertion, oxygen uptake, and heart rate at all stages of the treadmill are shown in Figures 1–3, respectively. The SLE patients had significantly lower submaximal oxygen uptake compared to controls (p = 0.05), but there were no significant differences in submaximal perceived exertion or heart rate between the groups.

Symptomatic measures. Total, physical, and mental fatigue were significantly greater in the SLE patients compared with controls (Table 4). Similarly, the SLE patients reported significantly worse sleep quality and significantly higher HAD anxiety and depression scores than the control group. The SLE patients were significantly more incapacitated than the controls on all SF-36 measures, particularly on the scales of role physical and role emotional.

Regression models. We obtained satisfactory models (reasonable variance explained and normally distributed residuals) for physical disability (SF-36 physical function scale and exercise duration) and for total fatigue measured using the VAS. The final model for physical function

Table 2. Clinical characteristics of patients with SLE and controls.

Variable	SLE Patients (n = 93)	Healthy Controls (n = 41)	p
Age (yrs)	39 (0.8)	37 (1.3)	0.09
Height (m)	1.62 (0.01)	1.61 (0.02)	0.71
Body mass (kg)	67.0 (58–75)	62 (57–69)	0.05
BMI	24.8 (22.3–28.9)	24.4 (21.4–27)	0.13
Total skinfold thickness (mm)	64.0 (2.6)	60.1 (3.4)	0.37
Waist/hip ratio	0.87 (0.01)	0.84 (0.02)	0.08
Caucasian (%)	52 (56)	28 (68)	0.37*
African-Caribbean (%)	22 (24)	6 (15)	
Asian (%)	19 (20)	7 (17)	
Smoker (%)	25 (27)	8 (20)	0.36*
In employment (%)	58 (62)	37 (90)	0.001*

Values are mean (SEM) or median (interquartile range). * Chi-square analysis was used.

Table 3. Physiological measurements.

Variable	SLE Patients (n = 93)	Healthy Controls (n = 41)	p
Test duration (min)	10.4 (0.4)	13.1 (0.6)	< 0.001
Peak oxygen uptake (ml/kg/min)	23.2 (0.7)	29.6 (0.8)	< 0.001
Maximum ventilation (1/min)	60.1 (1.8)	67.2 (2.4)	0.02
Peak respiratory exchange ratio	1.13 (0.01)	1.17 (0.01)	0.006
Maximum heart rate (beats/min)	171 (158–184)	182 (175–192)	< 0.001*
Recovery heart rate (beats/min)	102 (1.6)	107 (2.1)	0.07*
Predicted maximum heart rate (%)	94 (86–99)	99 (93–102)	0.001*
Maximum voluntary quadriceps contraction (N)	298 (13.5)	376 (23)	0.003
FEV_1 (l)	2.6 (0.07)	2.9 (0.08)	0.002
% predicted FEV_1	95 (1.8)	106 (2.3)	< 0.001
FVC (l)	2.9 (0.08)	3.2 (0.09)	0.006
% predicted FVC	92 (1.9)	101 (1.9)	0.001

Values are mean (SEM) or median (interquartile range).* The 3 patients taking β-blockers have been excluded from this analysis.

accounted for 53% of the variance in physical function, and the final model for exercise duration accounted for 61% of the variance in exercise duration (Table 5). The final model for fatigue accounted for 27 to 37% of the variance in fatigue, depending on which fatigue measure was used as the dependent variable (Table 6). There was a weak correlation between HAD depression and VO_{2peak} (Spearman test, r = –0.28, p = 0.008).

SLE patients. There were significant differences between the SLE patients who performed the test at 5 kph and those that performed the test at a slower speed because they were unable to walk at 5 kph (Table 7). Those able to do the test

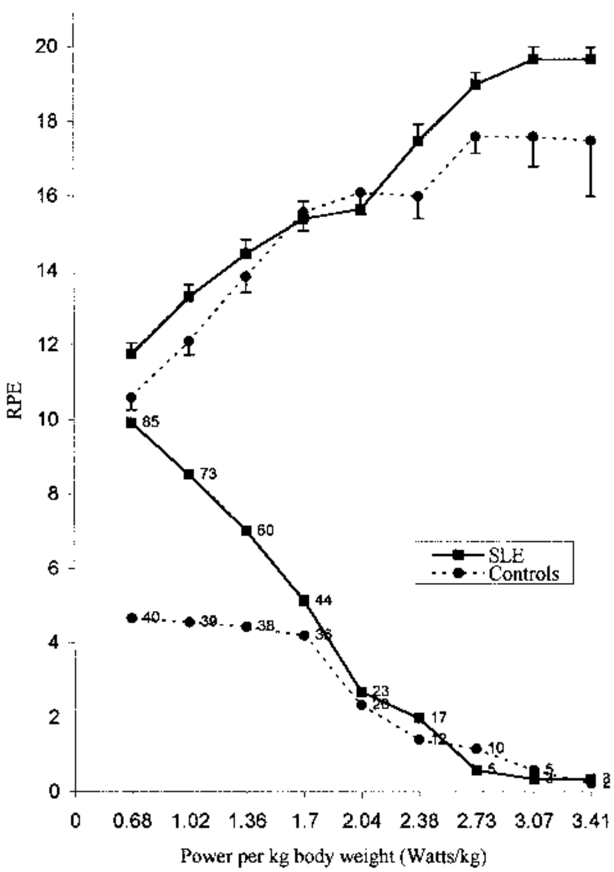

Figure 1. Submaximal rating perceived exertion (RPE) during the treadmill walking test. Mean (SEM shown as error bars). The lower 2 lines refer to the number of patients in each group at each treadmill stage.

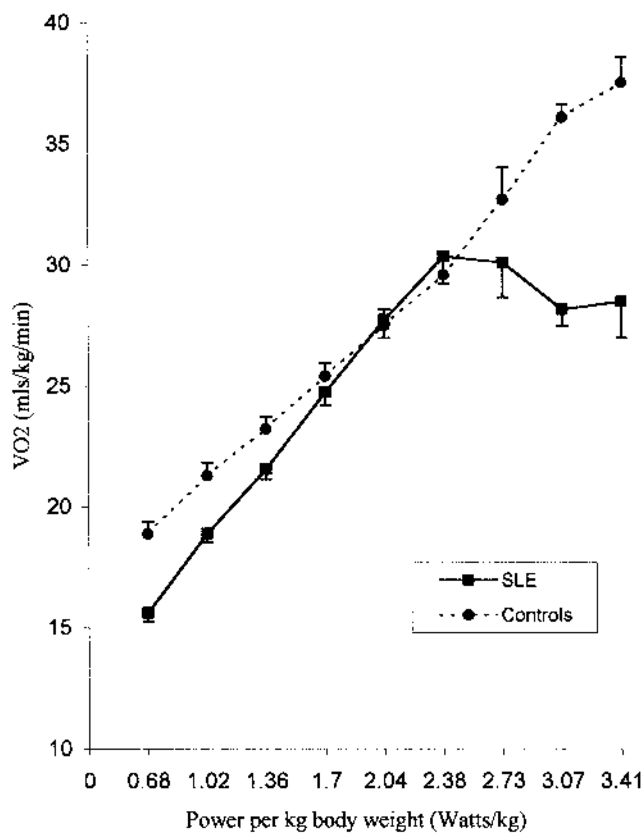

Figure 2. Submaximal oxygen uptake during the treadmill walking test. Mean (SEM shown as error bars).

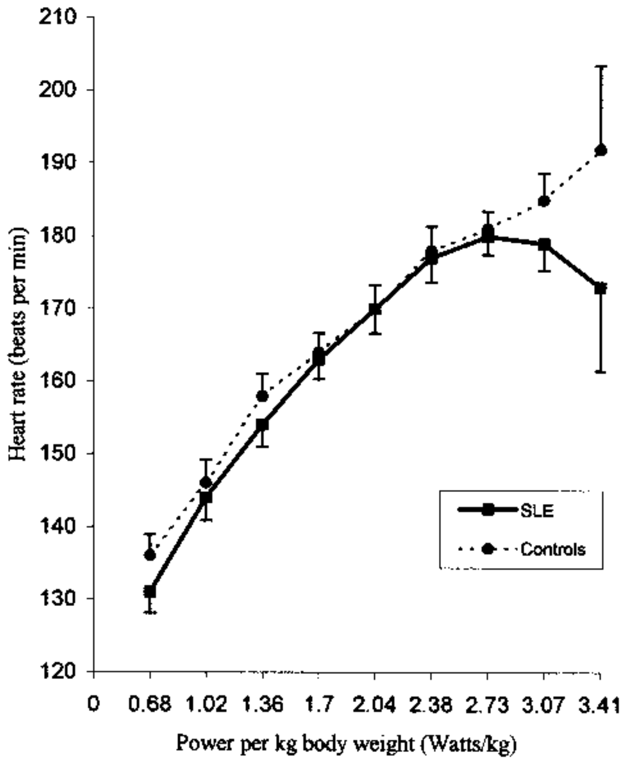

Figure 3. Submaximal exercise heart rate during the treadmill walking test. Mean (SEM shown as error bars). Three patients taking ß-blockers were excluded from this analysis.

at 5 kph were younger, had less active disease, a lower BMI, better lung function, greater isometric leg strength, and higher levels of aerobic fitness. Their physical function, role physical, and bodily pain scores were also higher; however, there were no significant differences in any of the other symptomatic measures.

DISCUSSION

There were no significant differences in potentially confounding variables between the 2 groups apart from body mass and employment status. The higher body mass in the SLE patients may have been in part due to steroid therapy. However, BMI provides a better reflection of body shape than mass alone and there was no difference in this variable between the groups. The individuals in the control group were sedentary but the working environment may have provided a possible source of exercise. However, no individuals in the control group were employed in jobs involving any heavy physical labor.

Symptomatic data. There was significantly more fatigue, worse sleep quality, and more depressed mood in the SLE patients compared to controls. Also, the low scores on the SF-36 scale indicate impaired function and disability in the SLE patients. These results are similar to those previously shown by us[1] and others[30].

Physiological data. Approximately one-quarter of the SLE patients performed the exercise test at a slower walking speed than the controls. The reason was that the 5 kph treadmill speed was too fast for some SLE patients and they

Table 4. Symptomatic measures.

Variable	SLE Patients (n = 93)	Healthy Controls (n = 41)	p
Fatigue Severity Score	5.67 (4.78–6.33)	3.33 (2.67–4.19)	< 0.001
Total fatigue	292 (6.5)	210 (5.6)	< 0.001
Mental fatigue	142 (3.5)	104 (3.6)	< 0.001
Physical fatigue	148 (3.5)	107 (3.2)	< 0.001
Chalder Fatigue Scale	23.5 (0.9)	15.0 (0.6)	< 0.001
PSQI sleep score	8 (5–12)	3 (2.5)	< 0.001
HAD			
Anxiety score	8 (6–12)	6 (4–10)	0.003
Depression score	7 (4–9)	3 (1–4)	< 0.001
SF-36			
Physical function	60 (45–80)	95 (83–100)	< 0.001
Role physical	25 (0–75)	100 (75–100)	< 0.001
Bodily pain	51 (31–79)	84 (72–100)	< 0.001
General health	40 (26–57)	72 (57–84)	< 0.001
Vitality	35 (20–53)	60 (48–73)	< 0.001
Social function	50 (37.5–75)	100 (75–100)	< 0.001
Role emotional	33.3 (0–100)	100 (66.7–100)	< 0.001
Mental health	64 (48–76)	76 (68–86)	< 0.001

Values are mean (SEM) or median (interquartile range). Normal or usual scores are up to 3 for the FSS, 14 for CFS, 200 for total VAS and 100 for physical and mental VAS. Score less than 8 on HAD scale is considered nonpathological. PSQI score less than 6 is considered nonpathological. 100 is the maximum (full capacity) SF-36 score for all subscales.

Table 5. Regression models for physical disability.

Dependent Variable	Independent Variable	β	SE	p	Adjusted R Square
Physical function	VO_{2peak}	1.41	0.32	< 0.001	0.35
	CFS	–0.82	0.27	0.003	0.47
	BMI	–0.94	0.36	0.01	0.51
	HAD depression	–1.24	0.61	0.05	0.53
Exercise duration	VO_{2peak}	0.30	0.05	< 0.001	0.57
	BMI	–0.19	0.07	0.008	0.59
	FSS	–0.36	0.17	0.04	0.61

FSS: Fatigue Severity Scale, CFS: Chalder Fatigue Scale, HAD: Hospital Anxiety and Depression Scale.

Table 6. Regression models for fatigue.

Dependent Variable	Independent Variable	β	SE	p	Adjusted R Square
VAS	HAD depression	8.02	1.38	< 0.001	0.32
	VO_{2peak}	–2.27	0.76	0.005	0.37
CFS	HAD depression	1.25	0.19	< 0.001	0.32
FSS	HAD depression	0.12	0.03	< 0.001	0.22
	PSQI	0.07	0.03	0.009	0.27

CFS: Chalder Fatigue Scale, HAD: Hospital Anxiety and Depression Scale, FSS: Fatigue Severity Scale, PSQI: Pittsburgh Sleep Quality Index.

could not maintain their position on the treadmill. For these individuals the work done at any given time point would be less than at a corresponding time point during a test performed at 5 kph. Therefore the test would, in theory, be easier and we might expect the patients who were tested at a slower walking speed to exercise for a longer time period before stopping due to exhaustion. Although this could influence the submaximal results, peak levels of all variables at volitional exhaustion should not be affected. By expressing the submaximal results according to power per kilogram of body weight rather than time on the treadmill, the problem of different treadmill speeds is avoided.

Inferior levels of aerobic fitness were demonstrated by a shorter treadmill time, lower VO_{2peak}, and lower maximum heart rate in the SLE patients compared to controls. The difference in treadmill time is likely to be an underestimate of the real difference because of the slower walking speed of some of the SLE patients. Exercise intolerance was demonstrated by a lower percentage of predicted maximum heart rate and a higher percentage of individuals with a peak

Table 7. Differences between SLE patients who performed the treadmill test at 5 kph and SLE patients who performed the test at a slower speed.

Variable	Treadmill Speed 5 kph (n = 68)	Treadmill Speed < 5 kph (n = 25)	p
Age (yrs)	38 (0.9)	43 (1.5)	0.006
BMI	24.0 (22–27)	28.4 (25–33)	< 0.001
Peak oxygen uptake (ml/kg/min)	25.5 (0.8)	16.7 (1.0)	< 0.001
Maximum voluntary quadriceps contraction (N)	322.9 (14.8)	232 (25.8)	0.002
FEV_1(l)	2.8 (0.1)	2.9 (0.1)	< 0.001
FVC (l)	3.1 (0.1)	2.3 (0.1)	< 0.001
SLAM	5.2 (0.34)	6.8 (0.65)	0.02
SF-36			
Physical function	66.9 (2.9)	46.2 (5.1)	< 0.001
Role physical	25 (0–75)	0 (0–25)	0.003
Bodily pain	51 (34–84)	41 (17–57)	0.01

Values are mean (SEM) or median (interquartile range).

respiratory exchange ratio < 1.1, indicating less than maximum effort when the test was terminated in the SLE patients compared to controls. This is an interesting finding and suggests that some of the SLE patients were unable to achieve maximum effort perhaps because of mental fatigue.

Another possible explanation for exercise intolerance and inferior levels of aerobic fitness is peripheral muscle deconditioning. The patients with SLE were physically weaker than the controls; however, isometric strength does not provide adequate information about muscle endurance and therefore may not reflect exercise capacity very closely.

Robb-Nicholson, *et al* showed a similar level of deconditioning in 23 SLE patients with a mean VO_{2peak} of 18.8 ml/kg/min and a mean percentage of predicted maximum heart rate of 91%[8]. Similarly, Daltroy, *et al* measured exercise time, but not oxygen uptake, during a graded exercise test on a bicycle ergometer in 35 patients with SLE and concluded that the SLE patients were deconditioned compared to age-sex norms[9]. Both of these studies were small and used published normative data as a comparison and neither measured resting pulmonary function. A study by Sakauchi, *et al* assessed factors limiting exercise capacity in patients with SLE[31]. They studied 21 patients with SLE and excluded those with cardiopulmonary complications determined by chest radiograph or echocardiogram. They found a low aerobic exercise capacity and concluded that this may have resulted from impaired oxygen diffusion in the inflamed peripheral muscles of patients with active SLE. Forte, *et al* studied 13 SLE patients with normal pulmonary function and concluded that reduced aerobic capacity is common in SLE and may be due to peripheral muscle deconditioning[32]. We did not exclude patients on the basis of abnormal pulmonary function tests and our results are therefore likely to be more representative of a typical outpatient population with SLE. Indeed, lung function abnormalities are very common even in asymptomatic patients. A study by Silberstein, *et al* found that up to 88% of unselected SLE patients were shown to have lung function abnormalities, with the most common abnormality being impairment in diffusing capacity[33]. Patients with pulmonary disease become short of breath with low or modest levels of activity and hence the low aerobic capacity in our group of patients may be partly explained by the impaired lung function limiting exercise tolerance rather than a peripheral muscle abnormality.

The submaximal data are difficult to interpret because of the different treadmill speeds. There was no difference in submaximal RPE or heart rate, suggesting that for most activities of daily living exercise intolerance should not be a limiting factor in patients with SLE.

Regression models. We chose to model the SF-36 physical function score as a self-perceived measure of physical disability, and exercise duration as a more objective measure of physical disability. We excluded patients from the exercise duration model who were unable to do the treadmill test at 5 kph because treadmill speed has an independent effect on exercise duration. The regression models for physical disability suggest that aerobic fitness, fatigue, a high BMI, and depression are important factors influencing physical disability in these patients. Aerobic fitness is likely to be the most reliable factor determining physical disability, as it was replicated in both models and explained the largest proportion of variability in each model. This suggests that exercise might be a useful treatment strategy in some patients with SLE. The regression model for fatigue explained only a third of the variance seen, with some variation according to which fatigue measure was used as the dependent variable. However, the data suggest that depression might be an important determinant of fatigue since it was replicated in all 3 models.

SLE patients. The differences between those patients who could perform the treadmill test at 5 kph and those who could not are not surprising and relate to differences in functional state rather than differences in fatigue severity, sleep quality, or mood disorder.

This work supports a hypothesis that fatigue and disability in SLE are related at least in part to poor levels of aerobic fitness, and that aerobic exercise may be a potential therapy for the treatment of fatigue and physical disability in SLE. We are presently carrying out a randomized, controlled trial of aerobic exercise on fatigue and sleep in SLE to explore this relationship.

ACKNOWLEDGMENT

We are grateful for the help and advice of Janice Thomas and John McCarthy.

REFERENCES

1. Tench CM, McCurdie I, White PD, D'Cruz DP. The prevalence and associations of fatigue in systemic lupus erythematosus. Rheumatology 2000;39:1249-54.
2. Krupp LB, LaRocca NG, Muir J, Steinberg AD. A study of fatigue in systemic lupus erythematosus. J Rheumatol 1990;17:1450-2.
3. Wysenbeek AJ, Leibovici L, Weinberger A, Guedj D. Fatigue in systemic lupus erythematosus. Prevalence and relation to disease expression. Br J Rheumatol 1993;32:633-5.
4. Zonana-Nacach A, Roseman JM, McGwin G Jr, et al. Systemic lupus erythematosus in three ethnic groups. VI: Factors associated with fatigue within 5 years of criteria diagnosis. LUMINA Study Group. Lupus in minority populations: nature vs nurture. Lupus 2000;9:101-9.
5. McKinley PS, Ouellette SC, Winkel GH. The contributions of disease activity, sleep patterns, and depression to fatigue in systemic lupus erythematosus. A proposed model. Arthritis Rheum 1995;38:826-34.
6. Middleton GD, McFarlin JE, Lipsky PE. The prevalence and clinical impact of fibromyalgia in systemic lupus erythematosus. Arthritis Rheum 1994;37:1181-8.
7. Taylor J, Skan J, Erb N, et al. Lupus patients with fatigue — is there a link with fibromyalgia syndrome? Rheumatology 2000;39:620-3.
8. Robb-Nicholson LC, Daltroy L, Eaton H, et al. Effects of aerobic

conditioning in lupus fatigue: a pilot study. Br J Rheumatol 1989;28:500-5.
9. Daltroy LH, Robb-Nicholson C, Iversen MD, Wright EA, Liang MH. Effectiveness of minimally supervised home aerobic training in patients with systemic rheumatic disease. Br J Rheumatol 1995;34:1064-9.
10. Tan EM, Cohen AS, Fries JF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271-7.
11. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus [letter]. Arthritis Rheum 1997;40:1725.
12. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The Fatigue Severity Scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. Arch Neurol 1989;46:1121-3.
13. Chalder T, Berelowitz G, Pawlikowska T, et al. Development of a fatigue scale. J Psychosom Res 1993;37:147-53.
14. White PD, Grover SA, Kangro HO, Thomas JM, Amess J, Clare AW. The validity and reliability of the fatigue syndrome that follows glandular fever. Psychol Med 1995;25:917-24.
15. Lewis G, Pelosi AJ, Araya R, Dunn G. Measuring psychiatric disorder in the community: a standardized assessment for use by lay interviewers. Psychol Med 1992;22:465-86.
16. Butler S, Chalder T, Ron M, Wessely S. Cognitive behaviour therapy in chronic fatigue syndrome. J Neurol Neurosurg Psychiatry 1991;54:153-8.
17. Fulcher KY, White PD. Randomised controlled trial of graded exercise in patients with the chronic fatigue syndrome. BMJ 1997;314:1647-52.
18. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193-213.
19. Ware JE, Sherbourne CD. The MOS 36-item Short-form Health Survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473-83.
20. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression scale. Acta Psychiatr Scand 1983;67:361-70.
21. Liang MH, Socher SA, Larson MG, Schur PH. Reliability and validity of six systems for the clinical assessment of disease activity in systemic lupus erythematosus. Arthritis Rheum 1989;32:1107-18.
22. Ward MM, Marx AS, Barry NN. Comparison of the validity and sensitivity to change of 5 activity indices in systemic lupus erythematosus. J Rheumatol 2000;27:664-70.
23. Gladman D, Ginzler E, Goldsmith C, et al. The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus. Arthritis Rheum 1996;39:363-9.
24. Ross W, Marfell-Jones M. Kinanthropometry. In: MacDougal J, Wenger HA, Green HJ, editors. Physiological testing of the high performance athlete. Champaign, IL: Human Kinetics Books; 1991:223-307.
25. Guidelines for the measurement of respiratory function. Recommendations of the British Thoracic Society and the Association of Respiratory Technicians and Physiologists. Respir Med 1994;88:165-94.
26. Borg G. Perceived exertion as an indicator of somatic stress. Scand J Rehabil Med 1970;2:92-8.
27. Stachenfeld NS, Eskenazi M, Gleim GW, Coplan NL, Nicholas JA. Predictive accuracy of criteria used to assess maximal oxygen consumption. Am Heart J 1992;123:922-5.
28. Fox E, Bowers R, Foss M. The physiological basis for exercise and sport. Dubuque, WI: Brown and Benchmark; 1993.
29. Jones DA, Newham DJ, Torgan C. Mechanical influences on long-lasting human muscle fatigue and delayed-onset pain. J Physiol 1989;412:415-27.
30. Bruce IN, Mak VC, Hallett DC, Gladman DD, Urowitz MB. Factors associated with fatigue in patients with systemic lupus erythematosus. Ann Rheum Dis 1999;58:379-81.
31. Sakauchi M, Matsumura T, Yamaoka T, et al. Reduced muscle uptake of oxygen during exercise in patients with systemic lupus erythematosus. J Rheumatol 1995;22:1483-7.
32. Forte S, Carlone S, Vaccaro F, et al. Pulmonary gas exchange and exercise capacity in patients with systemic lupus erythematosus. J Rheumatol 1999;26:2591-4.
33. Silberstein SL, Barland P, Grayzel AI, Koerner SK. Pulmonary dysfunction in systemic lupus erythematosus: prevalence, classification and correlation with other organ involvement. J Rheumatol 1980;7:187-95.