Physiologic Responses of Juvenile-Onset Diabetic Boys to Muscular Work

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SUMMARY

The cardiorespiratory and metabolic responses of juvenile-onset diabetic (Dia) and nondiabetic (Con) boys to light, moderate, and maximal treadmill work were investigated. No significant differences were observed between the Dia and Con subjects in cardiorespiratory responses to maximal and submaximal work. The mean values for the Dia boys during maximal treadmill work for ventilatory volume, oxygen uptake, heart rate, and lactic acid were 91.5 L/min, 54.9 ml/kg · min, 198 beats/min, and 7.0 mM/L, respectively. In the Dia boys, maximal-, light-, and moderate-intensity work produced significant plasma glucose decreases ($P < 0.05$) of 1.64, 3.23, and 7.2 mM/L, respectively. In the Con boys, the submaximal work bouts were performed without significant change in plasma glucose levels, but glucose levels after maximal work were elevated 1.58 mM/L. Light and moderate work in both groups produced no changes in plasma triglycerides, free fatty acids, or lactic acid. However, for the Dia boys, maximal work was associated with a significant increase of 0.36 mM/L in triglycerides.

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In 1926, Lawrence[1] reported that insulin and physical exercise produced a greater reduction in plasma glucose than did insulin alone. This finding has been verified by other investigators[2–4] and recently Koivisto and Felig[5] observed that the anatomic site of insulin injection before leg work will affect the magnitude of glucose reduction. In these investigations muscular work was conducted in the mornings and was preceded by insulin administration by up to 60 min. However, studies documenting the effects of insulin administered 8–10 h before muscular work conducted in the afternoons were limited to work bouts of short duration and low intensity[6,7] and several hours of cross-country skiing.[8]

Little information exists on the maximal oxygen uptake capacity of juvenile diabetics. Previous studies[9–11] with juvenile diabetics used the physical work capacity (PWC_{170}) test performed on a bicycle ergometer as a measure of aerobic power, and only one investigation[12] has reported on the maximum oxygen uptake of juvenile diabetic adolescents. With these considerations in mind, the cardiorespiratory and metabolic responses of insulin-dependent juvenile diabetics to maximal treadmill work and 60 min of submaximal walking, conducted 8–10 h after the morning insulin injection, were investigated.

METHODS

Subjects. Subjects in this investigation were 10 insulin-dependent juvenile-onset diabetic males and 10 age-matched nondiabetic males who acted as controls (Table 1).*

The diabetic and nondiabetic males were similar ($P > 0.05$) in height, body weight, body surface area (BSA), percent body fat, and pulmonary function. All the boys were of normal puberal status for their age. A preliminary review of the metabolic status of each subject was determined from a SMAC-20 analysis† done on a morning, fasting blood sample. Plasma concentrations of creatinine, BUN, CO_2, iron, triglycerides, total cholesterol, and cholesterol fractions of HDL and LDL were in the normal range for both groups. The mean fasting glucose level was 11.7 mM/L (range 6.39–21.2 mM/L) for the diabetics and 5.0 mM/L (range 4.33–5.61 mM/L) for the nondiabetics. The mean HbA_{1a+b+c} for diabetics was 13.0%, while in nondiabetics the value was 6.3%. None of the diabetics showed clinical

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* The nature and purpose of the study and the risks involved were explained verbally and given on a written sheet for each subject and his parents before their voluntary consent to participate. The protocol and procedures for this study were approved by the Human Subjects Committee of the Institute for Aerobics Research and the Southwestern Medical School, Dallas, Texas.
† Analysis performed on a Technicon AutoAnalyzer by Ford Medical Laboratories, Denton, Texas 76201.

TABLE 1
Physical characteristics of subjects

Subjects	Age (yr)	Height (cm)	Weight (kg)	BSA (m^2)	Bd. Fat (%)	FVC (L)	HbA_{1a+b+c} (%)	Duration insulin dependent (yr)	Insulin requirements			
									Morning Reg U	NPH U	Evening Reg U	NPH U
						Diabetics						
A	11	154.3	41.2	1.34	14.7	3.16	12.8	<1		14		4
B	12	154.9	48.8	1.45	12.3	3.36	9.3	3	11	22	5	10
C	12	146.7	36.5	1.22	6.6	2.48	12.6	3		24		
D	13	162.5	47.4	1.48	12.8	3.71	14.6	2	5	13	4	6
E	13	157.5	42.6	1.40	17.0	2.66	14.8	5		32		
F	13	158.1	50.9	1.50	14.2	3.11	15.0	12		58		
G	14	165.1	58.8	1.65	18.1	4.06	8.5	<1		27.5		
H	14	166.6	46.8	1.50	9.0	3.48	12.4	<1		24		
I	15	175.3	60.0	1.73	4.1	4.26	15.2	1		45		
J	15	172.7	58.9	1.70	7.7	3.99	14.3	9		76		
$\bar{X}$	13.2	161.4	49.19	1.50	11.65	3.43	13.0*					
SE	±0.42	±2.78	±2.55	±0.05	±1.46	±0.19	±0.8					
						Controls						
K	11	148.6	35.8	1.24	16.8	3.02	5.8					
L	12	152.4	46.9	1.41	19.6	3.60	6.3					
M	12	160.0	42.3	1.39	4.4	3.13	6.4					
N	13	164.4	52.7	1.57	13.3	3.72	6.1					
O	13	155.6	39.5	1.34	23.2	3.26	6.3					
P	13	162.6	65.2	1.70	18.4	3.72	7.2					
Q	14	160.0	43.0	1.41	7.1	2.93	5.9					
R	14	164.8	53.1	1.57	10.2	3.90	6.3					
S	15	172.7	55.8	1.67	10.6	4.20	6.2					
T	15	172.5	57.4	1.67	16.4	4.42	6.9					
$\bar{X}$	13.2	161.4	49.17	1.50	14.0	3.59	6.3					
SE	±0.42	±2.48	±2.90	±0.05	±1.87	±0.16	±0.14					

* Significant difference between groups ($P < 0.05$).

evidence of diabetic microangiopathy. The clinical records of the diabetics indicated that, except for the initial diagnosis of diabetes, none of the boys had been hospitalized for ketoacidosis or for a significant episode of hypoglycemia for at least 9 mo before the investigation. On the days of the treadmill tests the anatomic sites for the morning insulin injection varied in sequence and included the arm, abdomen, hip, and thigh. On these days each subject consumed his normal diet during the morning and noon meals.

Procedures. At 1-wk intervals, each subject performed a maximal incremental treadmill test and two 60-min walks of light and moderate intensity. All treadmill and inactivity trials were performed between 1400 and 1600 h in an ambient temperature of 23 ± 2°C and 50 ± 5% relative humidity. Lunch was consumed by participants approximately 2–3 h earlier.

Before the maximal test, each subject performed a pulmonary function test using an Ohio Medical spirometer; residual function was determined using the nitrogen washout procedure. Body density was determined by hydrostatic weighing, and body fat was calculated according to the formula of Brožek et al.[13] Body surface area was obtained from tables based on the DuBois height-weight formula.[14]

Each subject performed a maximal incremental treadmill test at a speed of 90m/min (3.3 mph) with the slope increasing 1.0% per minute. Oxygen uptake was measured during 5 min of seated rest and continuously throughout the work bout until the subject became exhausted. Ventilatory volumes were obtained from inspired air using a Parkinson-Cowan gasometer. Expired oxygen and carbon dioxide percentages were determined from mixed expired air using Beckman OM-11 and LB-2 gas analyzers, respectively. Calibration of the gas analyzers was checked periodically on a Lloyd-Gallenkamp gas analyzer. Heart rate was recorded the last 15 s of each minute of seated rest, muscular work, and for 5 min of seated recovery.

In addition, each subject performed two submaximal work bouts of 60-min duration at approximately 35% and 55% of maximal oxygen uptake capacity ($\dot{V}O_2$ max). During these tests oxygen uptake was determined for 5 min during seated rest and between minutes 10–15, 25–30, 40–45, and 55–60 of walking. Heart rate was recorded for the last 15 s of each minute of seated rest and for each 5-min segment of work. Body weight, rectal temperature using a clinical thermometer, and a 5-ml blood sample from the antecubital vein were obtained before and after each walking test. To control for the effect of posture on the concentration of plasma constituents,[15] the preexercise blood sample was obtained within 30 s of taking a seated position, after standing approximately 20 min. The postexercise samples were obtained 3 min after cessation of maximal work and within the first minute of completing each submaximal walking test. Each blood sample was analyzed for glucose, triglycerides, free fatty acids, lactic acid, hematocrit, and hemoglobin.

Blood glucose was analyzed in triplicate by the ortho-toluidine method.[16] Triglycerides, free fatty acids, and lactic acid were measured in duplicate by the methods of Dade,[17] Falholt et al.,[18] and Sigma,[19] respectively. The concentration of the unknown sample was derived from a comparison with standard solutions of known concentration run with each analysis. Hemoglobin (Hb) was determined in triplicate by the cyanmethemoglobin method. Hematocrit (Hct) was determined in triplicate by the microhematocrit method and corrected for 4% trapped plasma. Mean corpuscular hemoglobin concentration (MCHC) was calculated for hemoglobin and hematocrit. Percentage changes in plasma volume were calculated using Hct and Hb values.[20] Glycosylated hemoglobin was measured in duplicate by ion-exchange, column chromatography.[21] The analysis of covariance method from the General Linear Models Program of the Statistical Analysis System ($\alpha = 0.05$) was used to compare the changes in cardiorespiratory and hematologic variables between the groups across time.

RESULTS

The values for juvenile-onset diabetic and nondiabetic males for oxygen uptake, ventilatory volumes, ventilatory equivalent ratio, respiratory exchange ratio, oxygen pulse, and heart rate during maximal work are presented in Table 2.

No significant differences were observed between the diabetic and nondiabetic males in cardiorespiratory responses to maximal treadmill work. The mean values for the diabetics for maximal ventilatory volume, oxygen uptake, heart rate, and lactic acid were 91.5 L/min, 54.9 ml/kg · min, 198 beats/min, and 7.0 mM/L, respectively. Absolute maximal oxygen uptake (L/min) was highly related to body weight (r = 0.88) and height (r = 0.89), with the relationship to body surface area (BSA) giving the highest correlation (r = 0.93) (Figure 1). Maximal oxygen pulse also was highly correlated to BSA (r = 0.92).

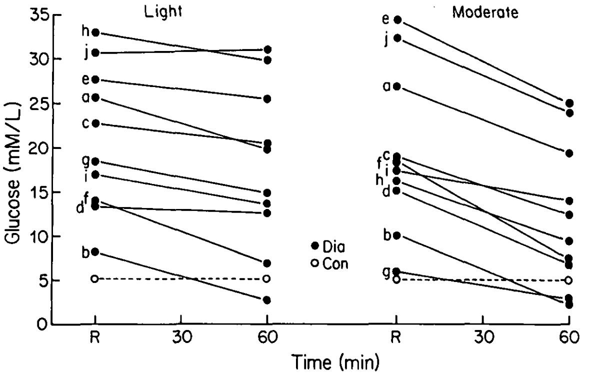

FIGURE 1. Maximum oxygen uptake (L/min) in relation to body surface area (BSA) in 10 diabetic (●) and 10 nondiabetic (○) males aged 11–15 yr. Linear regression equations relating body weight, height, and BSA to absolute $\dot{V}O_2$ max (L/min) are as follows: $\dot{V}O_2$ max (L/min) = 0.0518 (kg) + 0.1444; SEE = ±0.24; r = 0.88. $\dot{V}O_2$ max (L/min) = 0.054 (cm) − 6.018; SEE = ±0.23; r = 0.89. $\dot{V}O_2$ max (L/min) = 2.943 (BSA) − 1.716; SEE = ±0.19; r = 0.93.

No differences in oxygen uptake, respiratory exchange ratio, or heart rate were noted between the diabetic and nondiabetic males for seated rest before work or during 60 min of submaximal treadmill walking. During work of light and moderate intensity the diabetics had mean oxygen uptake

TABLE 2
Maximal values for pulmonary ventilations (V_E, BTPS), oxygen uptake (VO_2, STPD), ventilatory equivalent ratio (VE), respiratory ratio (R), heart rate, oxygen pulse, and lactic acid (LA) during maximal treadmill work for juvenile diabetics and controls

Subjects	$\dot{V}_E$ (L/min)	$\dot{V}O_2$ max (L/min)	$\dot{V}O_2$ max (ml/kg · min)	$\dot{V}O_2$ max* (ml/kg LBM · min)	VE	R	HR max (beats/min)	O_2 pulse (ml/beat)	LA (mM/L)
				Diabetics					
A	71.00	2.34	56.72	66.6	30.4	1.03	200	11.7	5.67
B	73.34	2.40	49.10	56.1	30.6	1.00	191	12.6	3.04
C	71.51	1.94	53.14	56.9	36.9	1.00	191	10.2	4.87
D	90.27	2.66	55.25	64.4	34.0	1.00	204	13.0	3.97
E	74.50	2.28	53.46	64.4	32.7	1.00	200	11.4	3.72
F	88.91	2.51	49.10	57.4	35.4	1.02	204	12.3	5.48
G	109.97	3.03	51.60	62.9	36.2	1.06	194	15.6	6.17
H	98.80	2.90	62.00	68.1	34.1	1.03	194	14.9	8.75
I	114.94	3.78	63.17	65.7	30.4	0.91	206	18.3	7.36
J	121.60	3.26	55.30	60.0	37.3	1.07	200	16.3	8.80
$\bar{X}$	91.48	2.71	54.88	62.25	33.8	1.01	198	13.6	5.73
SD	±6.05	±0.20	±1.51	±1.37	±0.85	±0.01	±2.0	±0.8	±0.64
				Controls					
K	73.67	2.04	57.00	68.4	36.1	1.04	200	10.2	5.58
L	100.20	2.57	54.83	68.2	39.0	1.10	202	12.7	8.28
M	68.30	2.19	51.73	54.2	31.2	1.03	185	11.8	3.74
N	98.36	2.91	55.30	63.7	33.8	1.02	200	14.6	6.74
O	61.30	2.23	55.80	73.6	27.4	1.00	206	10.8	4.60
P	109.00	3.02	46.25	56.8	36.1	1.03	200	15.1	7.29
Q	83.80	2.22	51.74	55.6	37.7	1.10	195	11.4	3.55
R	108.40	3.28	61.73	68.8	33.0	1.03	200	16.4	8.18
S	100.95	3.10	55.65	64.6	32.5	1.06	212	14.6	6.32
T	113.38	3.14	54.77	65.4	36.1	1.03	200	15.7	7.44
$\bar{X}$	91.74	2.67	54.48	63.93	37.3	1.04	200	13.3	6.12
SD	±5.88	±0.15	±1.27	±2.04	±3.0	±0.01	±2.0	±0.7	±0.54

$\dot{V}_E$, BTPS: ventilations corrected to body temperature pressure saturated.
$\dot{V}O_2$, STPD: ventilation values used for oxygen uptake were corrected to standard temperature pressure dry.
* Maximal oxygen uptake relative to kilograms of lean body mass (LBM).

TABLE 3
Plasma substrate concentrations for diabetic (Dia) and nondiabetic (Con) subjects before (pre) and after (post) maximal treadmill walking, 60 min of walking at light (35%) and moderate (55% $\dot{V}O_2$ max) intensities, and 60 min of seated inactivity*

		Maximal work		Light work		Moderate work		Seated inactivity (N = 7)	
Variable	Group	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Triglycerides	Dia	1.56 ± 0.40	1.92 ± 0.40†	1.59 ± 0.42	1.19 ± 0.29	1.32 ± 0.20	1.06 ± 0.20	1.16 ± 0.30	1.12 ± 0.18
(mM/L)	Con	1.30 ± 0.20	1.61 ± 0.20†	1.29 ± 0.12	1.28 ± 0.13	1.34 ± 0.14	1.48 ± 0.15	—	—
FFA (meq/L)	Dia	0.92 ± 0.15‡	1.07 ± 0.22‡	0.67 ± 0.12	0.59 ± 0.07	0.79 ± 0.11‡	0.56 ± 0.09	0.58 ± 0.08	0.57 ± 0.12
	Con	0.57 ± 0.07	0.57 ± 0.08	0.50 ± 0.04	0.54 ± 0.09	0.50 ± 0.06	0.70 ± 0.08	—	—
Lactic acid	Dia	1.19 ± 0.08	7.00 ± 0.70†	1.13 ± 0.07	0.85 ± 0.04	1.18 ± 0.08	1.31 ± 0.14	—	—
(mM/L)	Con	1.16 ± 0.07	7.60 ± 0.40†	1.07 ± 0.10	0.76 ± 0.04	1.10 ± 0.06	0.97 ± 0.06	—	—

* Data are presented as means ± SEM.
† Significant difference over time ($P < 0.05$).
‡ Significant difference between groups ($P < 0.05$).

values of 19.0 ml/kg · min (35.0% $\dot{V}O_2$ max) and 30.2 ml/kg · min (55.0% $\dot{V}O_2$ max), respectively, while the RQ (respiratory quotient) values at the 45th and 60th min of light and moderate work were 0.82 and 0.85, respectively. The steady-state heart rates (±SE) were 112 ± 2 and 142 ± 3 beats/min, respectively. Both groups had equivalent decreases in body weight with maximal (0.30), light (0.34), and moderate (0.43 kg) work and similar increases in rectal temperature with light (0.4) and moderate (0.8°C) walking.

Plasma substrate concentrations for diabetic and nondiabetic subjects for maximal and submaximal work are presented in Table 3 and Figures 2 and 3. In the diabetics, short-duration maximal work ($\overline{X}$ = 23 min 22 sec) and 1 h of walking at light and moderate intensities produced significant decreases in plasma glucose of 1.64 ± 0.62, 3.23 ± 0.70, and 7.2 ± 0.80 mM/L, respectively. These changes were unrelated to the morning or daily exogenous insulin dose of the subjects. In the nondiabetics, the submaximal work bouts were performed without significant change in plasma glucose values, but plasma glucose levels after the maximal tests were significantly elevated by 1.58 ± 0.40 mM/L.

Light and moderate work produced no change in plasma triglycerides or free fatty acids in either group. However, maximal work produced an increase in triglycerides of 0.36 mM/L in the diabetics and 0.31 mM/L in the nondiabetics.

In diabetics and nondiabetics, lactic acid increased to 7.00 ± 0.7 and 7.60 ± 0.4 mM/L with maximal work, respectively, but was unchanged by 1 h of submaximal walking. Maximal and submaximal work bouts also were associated with slight degrees of hemoconcentration and hemodilution, respectively, but these changes were not significant between groups or across time.

There were no significant relationships between aerobic capacity and plasma glucose levels at the start of exercise or with glycosylated hemoglobin levels.

DISCUSSION

Compared with age-matched nondiabetics, physical work capacity (PWC_{170}) has been reported to be lower in diabetic boys of shorter stature and lower body weight,[10] diabetic girls of equivalent height and higher body weight,[10] and diabetic boys of equivalent height and lower weight.[12] A lower $\dot{V}O_2$ max also has been reported for diabetic boys of similar height and lower body weight.[12] However, Larsson et al.[9] and Olavi et al.[11] found no difference in PWC_{170} between diabetic and nondiabetic children of the same physical size.

In our investigation diabetic and nondiabetic males were of the same body weight, height, and BSA and possessed equivalent values for maximal ventilatory volume, oxygen uptake, heart rate, and oxygen pulse. The high correlation coefficients of 0.88, 0.89, and 0.92 for body weight, height, and BSA with absolute $\dot{V}O_2$ max are similar in magnitude to the findings of earlier investigations in normal children and

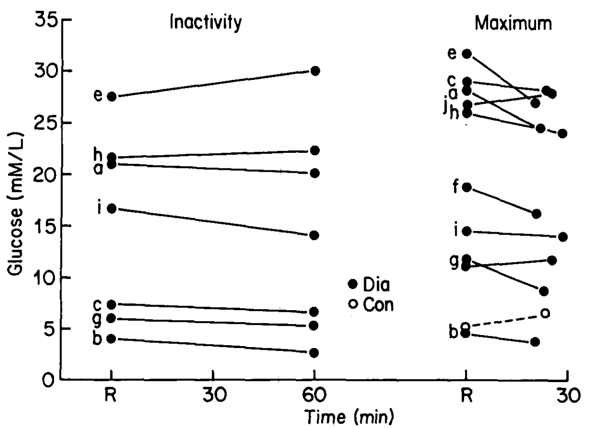

FIGURE 2. Venous glucose (mM/L) alterations in diabetic (●) and nondiabetic (○) males aged 11–15 yr with seated inactivity and treadmill work of maximal intensity. The letters (a–j) denote the individual diabetic subjects as shown in Tables 1 and 2.

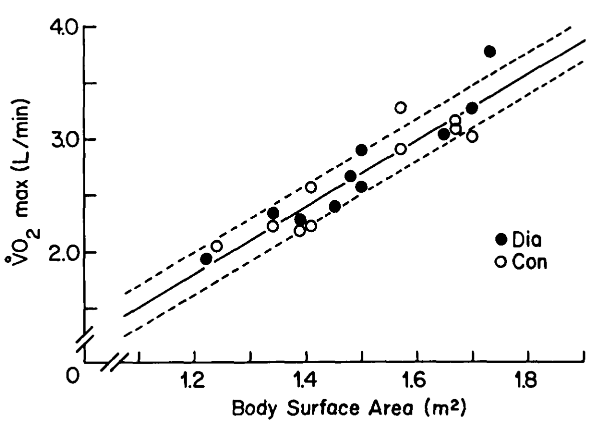

FIGURE 3. Venous glucose (mM/L) alterations in diabetic (●) and nondiabetic (○) males aged 11–15 yr with treadmill work of light and moderate intensities. The letters (a–j) denote the individual subjects as shown in Tables 1 and 2.

adults up to age 30 yr[22-25] and juvenile diabetics aged 7–20 yr.[8-12]

Several investigations reported the effect of the morning insulin injection on changes in plasma glucose levels with muscular work. The length of time of insulin administration before exercise and the duration and intensity of work performed includes 3 h before 60 min of free-play,[26] between 30 min and 2 h before cycle ergometry work (488–1347 kg/min),[2] 10 min before four 10-min work bouts at 75 W for females and 100 W for males,[5] 4 and 11 h before 0.5-mile walk at 4.0 mph up grades of 2.5% and 5.0%,[6] 60 min before 45 min of ergometry work at 50% $\dot{V}O_2$ max,[3,4] 2–4 h before a PWC_{170} test,[9,27] and 6 h before 3–4 h of cross-country skiing.[8] In these studies, fat oxidation during exercise was similar for diabetic and nondiabetic subjects, while in the diabetics exercise was associated with reductions in glucose levels that were related to the intensity,[2] amount of work conducted,[6] anatomic site of insulin injection,[5] intravascular and subcutaneous supply of insulin,[3-5] and level of plasma glucose before work.[6,8]

In our investigation, the average decrease in plasma glucose with maximal work of 1.64 mM/L was not related to the preexercise glucose level, but was similar in magnitude to the 2.8 mM/L reported by Karlefors[27] for similar type of work. In our subjects, 60 min of treadmill walking at 35% and 55% $\dot{V}O_2$ produced reductions of plasma glucose of 3.23 and 7.2 mM/L, respectively, compared with the findings of Larsson et al.,[8] who reported decreases in plasma glucose in six diabetic males, which ranged between 4.44 and 15.0 mM/L with 3–4 h of cross-country skiing. In our study, alterations in plasma glucose also were examined in seven of the diabetics after 60 min of seated inactivity. During this time the decrease in glucose was only -0.43 ± 0.7 mM/L ($P > 0.05$; Figure 2).

Koivisto and Felig[5] reported the effects of leg exercise on plasma glucose changes when the site of subcutaneous insulin injection was the arm, abdomen, and leg. These investigators found that glucose reduction rates were greatest when the injection site was the leg. In our investigation, the diabetic subjects administered their morning insulin injections in the arm, abdomen, thigh, and hip and performed treadmill work in the afternoons. Short-term maximal work and 60 min of light- and moderate-intensity walking produced progressively greater reductions in plasma glucose, which may be due to the intensity of the work bout. During the maximal test, work duration is relatively short due in part to the elevated production of lactic acid. During the submaximal work bouts, lactic acid production is lower and sufficiently buffered. Hence, the reduction in plasma glucose with submaximal work is related to the intensity of the work bout. Errebo-Knudsen[2] observed that decreases in plasma glucose accompanying leg work may not always start immediately, and Murray et al.[4] and Zinman et al.[3] reported that exercise-induced reductions in plasma glucose are the result of enhanced glucose utilization and decreased hepatic glucose production.

Several investigators reported the effect of insulin administered in the morning before exercise on changes in plasma lipids and ketones with physical work. Murray et al.[4] and Zinman et al.[3] observed that insulin administered subcutaneously 1 h before the start of ergometry work had little effect on free fatty acids and ketone levels, but was associated with an increase in glycerol during the 45 min of work. Vague et al.[7] observed depressed lipolysis in diabetics who performed 10 min of 80-W ergometry work 3.5 h after the noon meal. Larsson et al.[8] found that diabetics who performed three consecutive afternoons of 3–4 h of cross-country skiing had elevated free fatty acids before and after the work bouts. In our investigation, the RQ values at the 45th and 60th min of exercise and the postexercise values for free fatty acids, triglycerides, and lactic acid were equivalent in both groups during light and moderate work bouts. However, several of the diabetics of longer duration insulin dependency had free fatty acid levels that were slightly elevated before and after all work bouts.

The findings in this investigation suggest that juvenile-onset diabetics with a relatively short duration of insulin dependency and freedom from major vascular complications may possess aerobic work capacities equivalent to that of their age-matched nondiabetic counterparts of similar physical size. In diabetics, a maximal treadmill walking test and 60 min of walking at light and moderate intensities conducted 8–10 h after the morning insulin injection may be accompanied by progressive reductions in plasma glucose. These can produce a hypoglycemic reaction if plasma glucose levels are low before commencing exercise. There was no correlation between the ability to perform aerobic work and baseline plasma glucose or glycosylated hemoglobin levels.

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