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A 30-Year Follow-Up of the Dallas Bed Rest and Training Study

II. Effect of Age on Cardiovascular Adaptation to Exercise Training

Darren K. McGuire, MD, MHSc; Benjamin D. Levine, MD; Jon W. Williamson, PhD; Peter G. Snell, PhD; C. Gunnar Blomqvist, MD, PhD; Bengt Saltin, MD; Jere H. Mitchell, MD

Background—Aerobic power declines with age. The degree to which this decline is reversible remains unclear. In a 30-year longitudinal follow-up study, the cardiovascular adaptations to exercise training in 5 middle-aged men previously trained in 1966 were evaluated to assess the degree to which the age-associated decline in aerobic power is attributable to deconditioning and to gain insight into the specific mechanisms involved.

Methods and Results—The cardiovascular response to acute submaximal and maximal exercise were assessed before and after a 6-month endurance training program. On average, $\dot{V}O_{2\max}$ increased 14% (2.9 versus 3.3 L/min), achieving the level observed at the baseline evaluations 30 years before. Likewise, $\dot{V}O_{2\max}$ increased 16% when indexed to total body mass (31 versus 36 mL/kg per minute) or fat-free mass (44 versus 51 mL/kg fat-free mass per minute). Maximal heart rate declined (181 versus 171 beats/min) and maximal stroke volume increased (121 versus 129 mL) after training, with no change in maximal cardiac output (21.4 versus 21.7 L/min); submaximal heart rates also declined to a similar degree. Maximal AVDO₂ increased by 10% (13.8 versus 15.2 vol%) and accounted for the entire improvement of aerobic power associated with training.

Conclusions—One hundred percent of the age-related decline in aerobic power among these 5 middle-aged men occurring over 30 years was reversed by a 6-month endurance training program. However, no subject achieved the same maximal $\dot{V}O_2$ attained after training 30 years earlier, despite a similar relative training load. The improved aerobic power after training was primarily the result of peripheral adaptation, with no effective improvement in maximal oxygen delivery. (*Circulation*. 2001;104:1358-1366.)

Key Words: aging ■ oxygen ■ exercise ■ cardiac output ■ heart rate

In 1966, 5 healthy, 20-year-old men were studied extensively at baseline, after 3 weeks of bed rest, and after 8 weeks of intensive dynamic exercise training. The results of this original investigation as well as data from 30-year follow-up baseline evaluations of these same 5 men have been published.^{1,2} The present study was designed to investigate the cardiovascular adaptations to exercise training in these 5 middle-aged men. This investigation sought to assess the degree to which the age-associated decline in aerobic power that was documented in the baseline follow-up evaluations is attributable to physical inactivity and deconditioning and to gain insight into the specific mechanisms contributing to any observed recovery of aerobic power.

The decline in cardiovascular capacity associated with aging has been well documented in prior reports,³⁻⁹ including previous evaluations of the subjects who participated in the present study.^{1,2} However, within this literature, there are few

longitudinal evaluations over extended intervals; the mechanisms responsible for the decline in aerobic power remain poorly understood; and the degree to which the age-related changes are reversible remains unclear.^{2,6,10-12} The present study represents one of the longest longitudinal evaluations reported to date and is unique in describing the effects of two endurance training programs separated by a long period of time. The purpose of this study was to assess the effects of endurance training in these healthy, middle-aged men; to compare the training response with that observed 30 years before, after a comparable regimen of endurance training; and to compare the mechanisms of cardiovascular adaptation observed during these evaluations separated by a 30-year interval.

Methods

The subjects were 5 healthy men, 50 to 51 years of age, who were originally studied by 3 of the present investigators (B.S., C.G.B.,

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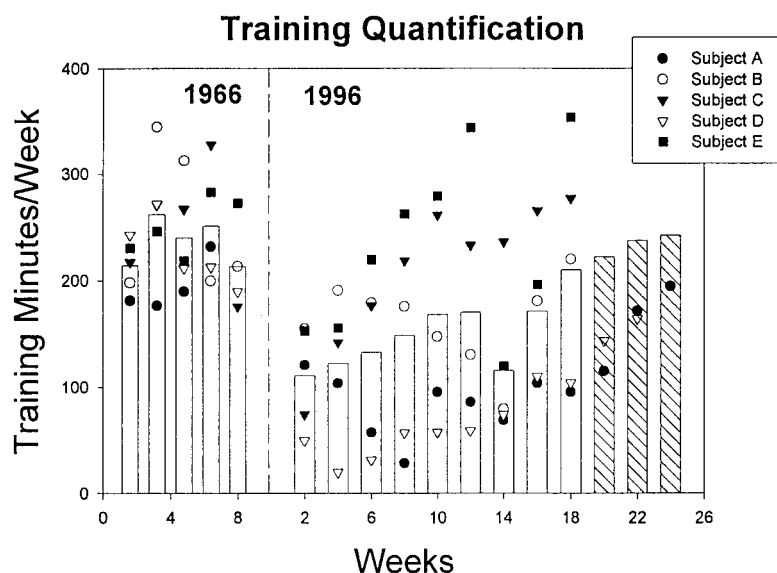


Figure 1. Individual and group exercise duration during the 1966 and present training programs, with each bar graph representing mean weekly training duration. Because subjects completed prescribed training at different times in the current study, over the final 6 weeks, hatched bars reflect mean training duration of the whole group, with the final week's training duration carried forward for "average" calculations for those finishing previously. Thus, last hatched bar represents mean peak training duration for all subjects at time of completion of their training, immediately before testing.

J.H.M.) in 1966. All participants provided informed consent to a protocol approved by the University of Texas Southwestern Medical Center Institutional Review Board. These subjects are characterized in detail previously, as are the methods of baseline screening and evaluation.²

Exercise Training

After baseline cardiopulmonary evaluations at rest and in response to graded exercise testing, the subjects underwent a structured endurance training program. With the use of data from the original study in 1966, exercise targets were determined for each subject in an effort to reproduce that "dose" (frequency, duration, and intensity) of endurance exercise achieved in the original study and to maintain that level of exercise for at least 1 week before the final evaluations. The objective of the exercise prescription was to begin modestly, with progressive titration of exercise dose over the planned 6-month period. Given the risk and consequences of injury in this small group of middle-aged subjects, we did not reproduce the high-intensity "interval" training portion of the 1966 exercise program. Subjects used wristwatch-style heart rate monitors (Polar Vantage XL) to adjust their exercise intensity to target heart rates and to electronically record each exercise session. Files from the heart rate monitors were downloaded weekly; based on these data, exercise prescription was individually titrated throughout the training period with the intention of incrementing net weekly duration by 5% to 10% each week at a fixed intensity of $\approx 75\%$ maximal heart rate.

Posttraining Assessments

After completion of the training period, all subjects underwent identical assessments as had been performed at baseline with methods described previously.² Briefly, subjects underwent cardiopulmonary assessments at rest and at 2 steady-state levels of submaximal treadmill exercise at $\approx 60\%$ and 80% maximal effort (individually determined), with the same absolute workloads used as in the baseline evaluations. After a period of rest, subjects performed a maximal graded treadmill exercise test with the same assessments performed. This strategy reproduced the evaluations performed in 1966 and included assessments of heart rate (ECG), blood pressure, oxygen uptake (Douglas Bag technique), cardiac output (acetylene rebreathing), and arterialized lactate under each of the conditions described.^{1,2} In addition to the evaluations of 1966, 3 of 5 subjects underwent gated cardiac MRI before and after training with the use of techniques standard at our institution.¹³

Results

All 5 subjects completed the prescribed exercise program within the planned 6-month period without injury or compli-

cation and maintained their target level of exercise for at least 1 week before the final evaluations. A summary of the progressive dose of exercise during the training program is presented in Figure 1, along with comparative data from the 1966 study. On average, intensity of exercise during the final week in the present study was 77% of maximal heart rate, compared with 88% maximal heart rate (HR_{max}) in the final week of training in 1966. The period of training required to achieve the goal ranged from 18 to 24 weeks, with a mean of 19.6 weeks.

Group Average Results

Average pretraining and posttraining baseline characteristics are presented in Table 1, along with comparative data from 1966. In comparing pretraining versus posttraining values, there was little change in body weight (100 versus 96 kg), percent body fat (28% versus 30%), or fat-free mass (FFM, 69.4 versus 64.8 kg). There was a 14% decrease in resting heart rate (90 versus 77 beats/min) as well as decreases in resting systolic (140 versus 132 mm Hg) and diastolic (88 versus 84 mm Hg) blood pressure. End-diastolic total cardiac volume in the 3 subjects who underwent cardiac MRI (left ventricular [LV] and right ventricular [RV] volumes and mass, comparable to but more precise than the quantitative radiographic volumes measured in 1966) was similar before and after training (637 versus 646 mL).

All subjects achieved maximal exertion on exercise testing before and after training (Table 2). Group average results from the posttraining cardiopulmonary exercise testing are presented in Table 3.

In comparing pretraining and posttraining data, a number of trends were evident. At each level of submaximal exercise, oxygen uptake ($\dot{V}O_2$) was unchanged; cardiac output (CO) was slightly lower with lower HR balanced by increased stroke volume (SV); and total peripheral resistance (TPR) and arteriovenous oxygen difference ($AVDO_2$) were largely unchanged (Table 3). The relation between $\dot{V}O_2$ and other hemodynamic parameters across the spectrum from rest to maximal exertion over the 30-year interval are depicted in

TABLE 1. Baseline Characteristics: Group Averages

	1966		1996	
	Baseline	After Training	Baseline	After Training
Height, cm	184 (3.3)		185 (1.6)	
Weight, kg	77 (15)	77 (13)	100 (37)	96 (37)
%Body fat	14 (4.1)	13 (4.2)	28 (3.0)	30 (8.6)
Systolic blood pressure, mm Hg	131 (23)	144 (9)	140 (4)	132 (14)
Diastolic blood pressure, mm Hg	75 (14)	78 (6)	88 (7)	84 (6)
MAP, mm Hg	94 (17)	100 (6)	105 (6)	100 (6)
HR, beats/min	76 (27)	57 (10)	90 (17)	77 (17)
$\dot{V}O_2$, L/min	0.3 (0.04)	0.3 (0.05)	0.4 (0.13)	0.4 (0.14)
$\dot{V}O_2$, mL/kg per minute	4.3 (0.7)	4.2 (0.5)	3.7 (0.2)	3.7 (0.4)
$\dot{V}O_2$, mL/kg FFM per minute	5.0 (0.8)	4.9 (0.6)	5.2 (0.3)	5.3 (0.6)
CO, L/min	5.7 (1.3)	4.4 (0.8)	5.9 (1.1)	5.5 (1.1)
SV, mL/min	79 (23)	77 (4)	68 (18)	75 (19)
AVDO ₂ , mL O ₂ /100 mL blood	5.8 (1.2)	7.9 (1.2)	6.1 (1.2)	6.3 (1.2)
Hematocrit, %	44	43	47	48
MRI cardiac volume*	N/A	N/A	637 (111)	646 (122)

Values are given as means (SD). %Body fat was determined by underwater weighing technique.

*Three of 5 subjects (B, C, D) underwent cardiac MRI.

Figure 2. Importantly, the relation between CO and $\dot{V}O_2$ across the range of effort was not altered despite the 30-year interval, before or after training (Figure 2A).

Absolute $\dot{V}O_{2max}$ increased by 14% (2.9 versus 3.3 L/min) (Figure 3), a change in magnitude similar to the 18% increase observed after training in 1966. Likewise, increases were observed in $\dot{V}O_{2max}$ indexed to total body mass (31.0 versus 35.9 mL/kg per minute) and indexed to FFM (43.7 versus 51.2 mL/kg FFM per minute) (Figure 4). On average, there was no change in CO_{max} (21.4 versus 21.7 L/min), with a 6% decline in HR_{max} (181 versus 171 beats/min) balanced by a 7% increase in SV_{max} (121 versus 129 mL) (Figures 5 through 7). Therefore, a 10% improvement in AVDO_{2max} (13.8 versus 15.2 vol%) accounted for the improvement in aerobic power (Figure 8). There was no change in maximal mean arterial pressure (MAP_{max}) (134 versus 133 mm Hg) or TPR_{max} (523 versus 518 dyne · s⁻¹ · cm⁻⁵) (Figure 9).

In comparing posttraining data from 1966 versus 1996, absolute $\dot{V}O_{2max}$ declined by 15% over the 30-year interval (3.9 versus 3.3 L/min) (Table 3 and Figure 3). Likewise, declines were observed in maximal oxygen uptake indexed to total body mass (51.1 versus 35.9 mL/kg per minute) and indexed to FFM (59.7 versus 50.5 mL/kg FFM per minute) (Figure 4). Declines were observed in CO_{max} (22.8 versus 21.7

L/min) and HR_{max} (190 versus 171 beats/min), with an increase in SV_{max} (120 versus 129 mL) (Figures 5 through 7). TPR_{max} was increased (417 versus 518 dyne · s⁻¹ · cm⁻⁵) and AVDO_{2max} decreased (17.1 versus 15.2 vol%) (Figures 8 and 9).

Individual Results

Comprehensive demographic, anthropometric, and cardiovascular data for the individual subjects are published in Circulation Online as Tables A-E [REFERENCE], including comparative data from 1966 in addition to the current results.

Subject A completed the prescribed exercise program in 24 weeks, walking 22.4 miles in 276 minutes in the final week at an average of 72% maximal heart rate in 4 exercise sessions. Absolute $\dot{V}O_{2max}$ increased 24% (2.1 versus 2.6 L/min) (Figure 3), and, indexed to FFM, $\dot{V}O_{2max}$ increased 36% (33.7 versus 45.7 mL/kg FFM per minute). A 10% decline in CO_{max} (15.8 versus 14.2 L/min) (Figure 5) resulted from a decline primarily in HR_{max} (197 versus 181 beats/min) (Figure 6), with no real change in SV_{max} (80 versus 77 mL) (Figure 7) and a 6% decrease in TPR_{max} (734 versus 684 dyne · s⁻¹ · cm⁻⁵) (Figure 9). The entire improvement in aerobic performance resulted from a 43% increase in AVDO_{2max} (12.9 versus 18.5 vol%) (Figure 8).

TABLE 2. Confirmation of Maximal Exercise Testing at Evaluations Before and After Training

	Subject A		Subject B		Subject C		Subject D		Subject E	
	Before	After	Before	After	Before	After	Before	After	Before	After
Respiratory exchange ratio	1.21	1.01	1.17	1.08	1.18	1.14	1.14	1.11	1.10	1.07
$\dot{V}E/\dot{V}O_2$	45.0	47.8	34.9	32.3	46.7	49.6	36.5	34.4	41.2	42.5
Arterialized lactate, mmol/L	10.6	9.0	7.0	8.2	10.0	9.6	8.6	6.4	8.2	6.7
%Maximal predicted HR	115	109	99	97	112	105	111	102	94	91

$\dot{V}E/\dot{V}O_2$ indicates rate of expired ventilatory volume/rate of ventilatory oxygen uptake.

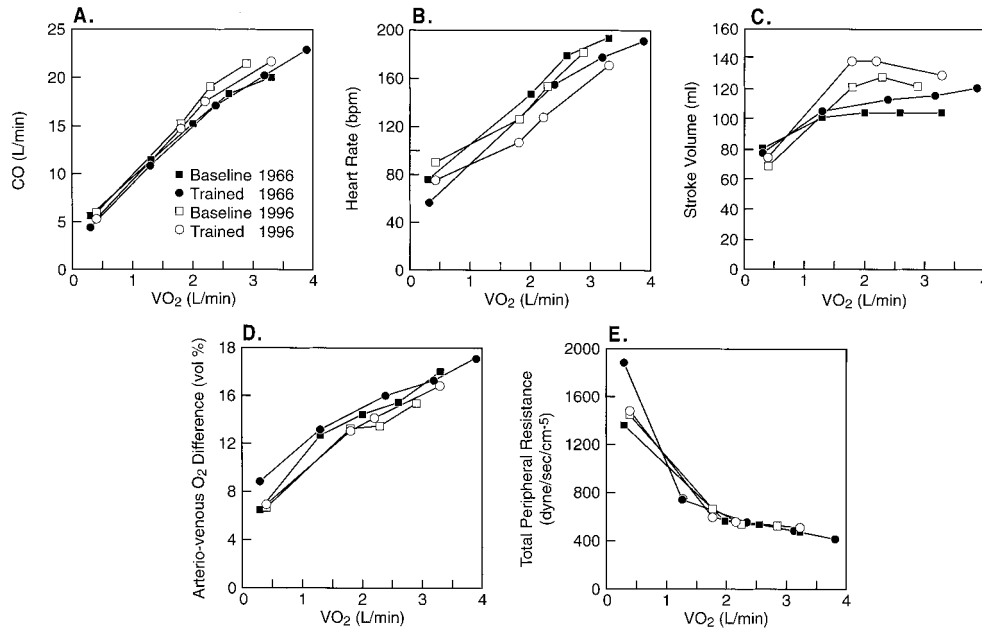


Figure 2. Relation of various hemodynamic parameters to oxygen uptake across range of exercise from rest to maximal effort at baseline and after training from both 1966 and the present study, presented as group mean data. A, Cardiac output; B, heart rate; C, stroke volume; D, arteriovenous oxygen difference; E, total peripheral resistance.

Subject B completed the prescribed exercise program in 18 weeks, jogging 25 miles in 214 minutes in the final week at an average of 77% maximal heart rate in 5 exercise sessions. Absolute $\dot{V}O_{2\max}$ increased 12% (3.7 versus 4.1 L/min) (Figure 3), and, indexed to FFM, $\dot{V}O_{2\max}$ increased 18% (55.8 versus 66.1 mL/kg FFM per minute). CO_{\max} increased 11% (25.0 versus 27.8 L/min), with little change in HR_{\max} (168 versus 164 beats/min), and a 14% increase in SV_{\max} (149 versus 170 mL) (Figures 5 through 7). There was no change in $AVDO_{2\max}$ (14.6 versus 14.7 vol%) and a 26% decrease in TPR_{\max} (491 versus 362 dyne \cdot s⁻¹ \cdot cm⁻⁵) (Figures 8 and 9).

Subject C completed the prescribed exercise program in 17 weeks, and he was the only subject who chose to train on a stationary cycle ergometer. However, testing was on a treadmill, similar to the other subjects. In the final week, he pedaled for 285 minutes at an average of 80% maximal heart rate in 4 exercise sessions. Absolute $\dot{V}O_{2\max}$ (measured on a treadmill) declined 7% (2.8 versus 2.6 L/min) (Figure 3), and, indexed to FFM, $\dot{V}O_{2\max}$ was unchanged (47.2 versus 47.8 mL/kg FFM per minute). CO_{\max} increased 14% (16.4 versus 18.7 L/min) (Figure 5) with a 6% decrease in HR_{\max} (190 versus 178 beats/min) and a 22% increase in SV_{\max} (86 versus 105 mL) (Figures 6 and 7). In contrast to the other subjects, this was the only individual who had a decline in $AVDO_{2\max}$ (16%; 16.8 versus 14.1 vol%; Figure 8). TPR_{\max} increased 4% (572 versus 596 dyne \cdot s⁻¹ \cdot cm⁻⁵; Figure 9).

Subject D completed the prescribed exercise program in 21 weeks, jogging 16 miles in 164 minutes in the final week at an average of 74% maximal heart rate in 4 exercise sessions. Absolute $\dot{V}O_{2\max}$ increased 11% (2.7 versus 3.0 L/min) (Figure 3), as did $\dot{V}O_{2\max}$ indexed to FFM (33.7 versus 45.7 mL/kg FFM per minute). There was no change in CO_{\max} (22.6 versus 22.0 L/min), with an 8% decline in HR_{\max} (189 versus 173 beats/min) balanced by a 6% increase in SV_{\max} (120 versus

127 mL) (Figures 5 through 7). The entire improvement in aerobic performance resulted from a 15% increase in $AVDO_{2\max}$ (11.7 versus 13.4 vol%) (Figure 8). TPR_{\max} increased 27% (441 versus 561 dyne \cdot s⁻¹ \cdot cm⁻⁵) (Figure 9).

Subject E completed the prescribed exercise program in 18 weeks, walking 20.2 miles in 308 minutes in the final week at an average of 84% maximal heart rate in 7 exercise sessions. Absolute $\dot{V}O_{2\max}$ increased 14% (3.5 versus 4.0 L/min) (Figure 3), and, indexed to FFM, $\dot{V}O_{2\max}$ increased 29% (33.2 versus 42.8 mL/kg FFM per minute). CO_{\max} declined 5% (27.0 versus 25.7 L/min), with a 4% decline in HR_{\max} (160 versus 154 beats/min) and no change in SV_{\max} (169 versus 167 mL) (Figures 5 through 7). The entire improvement in aerobic performance resulted from a 19% increase in $AVDO_{2\max}$ (13.0 versus 15.5 vol%) (Figure 8). TPR_{\max} was unchanged (375 versus 384 dyne \cdot s⁻¹ \cdot cm⁻⁵; Figure 9).

Discussion

The most notable findings of the study include (1) 6 months of endurance training restored 100% of the age-associated decline in aerobic power previously documented in these same 5 men over the 30-year study interval^{1,2}; (2) despite this training effect, no individual achieved the level of aerobic power achieved after training 30 years previously; (3) the mechanism of recovery of aerobic power predominantly involved a peripheral adaptation to training evidenced by increased $AVDO_{2\max}$, with no change in CO_{\max} ; and (4) the relation of CO to $\dot{V}O_2$ remained unchanged after 6 months of endurance training and after 30 years of aging.

Aerobic power declines with age,²⁻⁹ but little information is available addressing the mechanisms of the decline, especially the influence of progressive physical inactivity and resultant deconditioning. The current training study, spanning 3 decades, represents one of the longest longitudinal studies

TABLE 3. Results of Submaximal and Maximal Treadmill Exercise Testing

	1966		1996	
	Baseline	After Training	Baseline	After Training
HR, beats/min				
Submax 1	147	155	126	108
Submax 2	178	177	153	129
Maximal	193	190	181	171
Systolic blood pressure, mm Hg				
Submax 1	169	193	183	156
Submax 2	199	194	184	179
Maximal	204	201	208	192
Diastolic blood pressure, mm Hg				
Submax 1	74	76	87	87
Submax 2	85	78	91	89
Maximal	81	74	96	103
MAP, mm Hg				
Submax 1	106	115	119	110
Submax 2	123	117	122	119
Maximal	122	116	134	133
$\dot{V}O_2$, L/min				
Submax 1	2.0	2.4	1.8	1.8
Submax 2	2.6	3.2	2.3	2.2
Maximal	3.3	3.9	2.9	3.3
$\dot{V}O_2$, mL/kg FFM per minute				
Submax 1	30.1	36.9	26.8	28.2
Submax 2	38.8	47.4	34.3	35.3
Maximal	49.7	59.7	43.7	51.2
$\dot{V}O_2$, mL/kg per minute				
Submax 1	26.0	31.5	19.0	19.9
Submax 2	33.6	40.8	24.3	24.8
Maximal	43.0	51.1	31.0	35.9
CO, L/min				
Submax 1	15.2	17.1	15.1	14.9
Submax 2	18.3	20.2	19.0	17.6
Maximal	20.0	22.8	21.4	21.7
SV, mL				
Submax 1	104	112	121	138
Submax 2	104	115	127	138
Maximal	104	120	121	129
Max AVDO ₂ , mL O ₂ /100 mL blood				
Submax 1	13.0	14.4	11.9	11.8
Submax 2	13.9	15.5	12.1	12.8
Maximal	16.2	17.1	13.8	15.2
TPR, dyne · s ⁻¹ · cm ⁻⁵				
Submax 1	573	557	665	604
Submax 2	543	483	538	568
Maximal	484	417	523	518

Values are given as means.

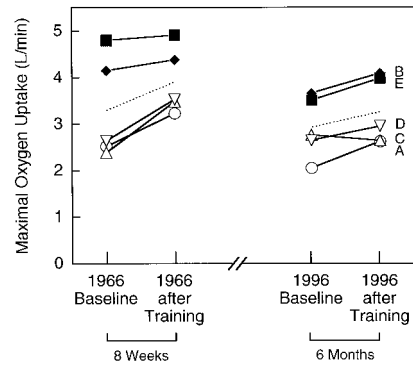


Figure 3. Absolute maximal oxygen uptake (L/min) before and after training in 1966 and in 1996.

reported evaluating the effect of aging on the cardiovascular response to endurance training in healthy middle-aged men.

Training Compliance

All subjects completed the prescribed training program within the planned study interval without limiting injury or complications. The high degree of compliance without injury probably is the result of multiple features of our training strategy that followed current professional guidelines regarding physical activity prescription.^{14,15} First, subjects were allowed to choose the mode of exercise they enjoyed. Second, the initial training dose was mild, allowing subjects to accommodate to the training program before attempting more rigorous exercise. Third, the use of wristwatch-style heart rate monitors allowed the subjects to adjust the intensity of their training sessions and probably prevented overly intense exercise that often results in exhaustion, soreness, injury, and resultant noncompliance. Moreover, they also allowed us to accurately document the dose of training for each subject for direct comparison with the 1966 data. Fourth, weekly adjustment of the individualized training prescription maintained a gradual but constant increase in the training dose and provided an opportunity for positive feedback and encouragement from the investigators. The observed 16% improvement in aerobic power (indexed to FFM) objectively demonstrates the effectiveness of our training strategy and is consistent with the results from other endurance training studies of healthy, nonathletic, middle-aged adults.¹⁶⁻¹⁹

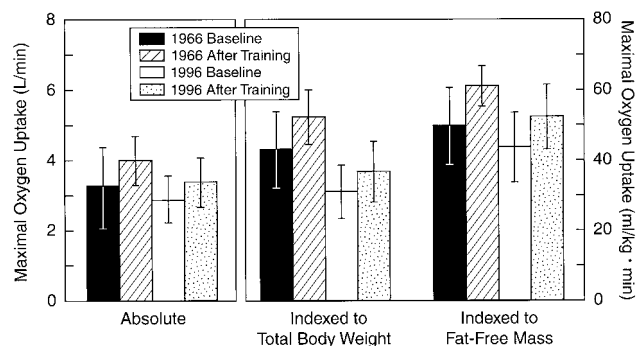


Figure 4. Maximal oxygen uptake (L/min) from 1966 and the present study reported as absolute values, indexed to present body weight, and indexed to fat-free body mass.

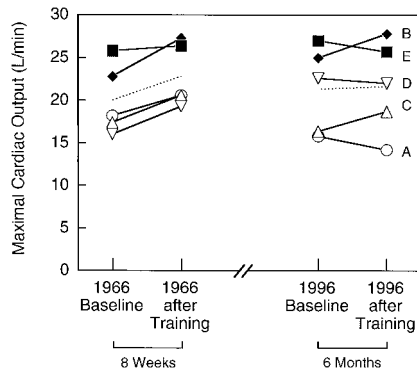


Figure 5. Maximal cardiac output (L/min) before and after training in 1966 and in 1996.

Anthropometric Effects of Training

Despite 6 months of endurance training, on average, only a 4-kg decline in body weight (100 versus 96 kg) and a $1.1\text{-kg} \cdot \text{m}^{-2}$ decrease in body mass index (29.1 versus $28.0 \text{ kg} \cdot \text{m}^{-2}$) were observed after training, with no change in percent body fat. Although modest, the magnitude of the anthropometric changes are consistent with most prior training studies of adult men.^{20,21} These observations suggest that the increased energy expenditures of training were accompanied by a concomitant increase in caloric intake, underscoring the importance of dietary prescription as an adjunct to physical exercise if weight loss is a desired outcome.

Submaximal Exercise Comparisons

Comparisons of submaximal exercise testing results demonstrate some of the cardiovascular effects associated with endurance exercise and are consistent with prior training studies of adult men.^{12,16,17,22} At each submaximal level of testing, performed at the same absolute work rate before and after training, $\dot{V}O_2$ was unchanged, suggesting that there was no significant change in exercise efficiency associated with training. After training, a prominent decline in HR, more than was observed during training in youth, was balanced by an increased SV at rest and at both levels of submaximal effort, resulting in no effective change in CO. There were also no significant changes in $AVDO_2$ or TPR during submaximal evaluations, emphasizing that when CO was not limited,

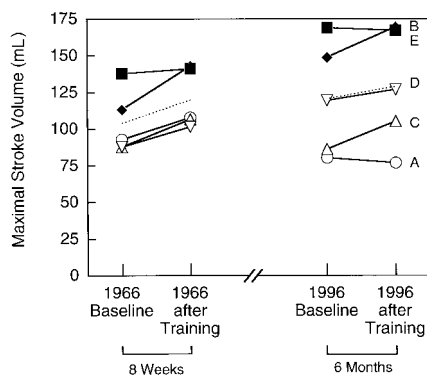


Figure 6. Maximal stroke volume (mL) before and after training in 1966 and in 1996.

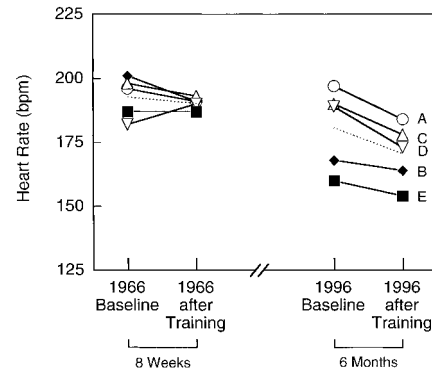


Figure 7. Maximal heart rate (beats/min) before and after training in 1966 and in 1996.

peripheral adjustments were not necessary to maintain normal levels of oxygen utilization.

Thus, in 1966 and in the current study, there was a highly correlated linear relation between CO and $\dot{V}O_2$ that was not altered by exercise training. These observations are consistent with previous studies,^{1,12,17,18} but little longitudinal information is available regarding the stability of the CO/ $\dot{V}O_2$ relation over extended intervals. We observed no significant change in this linear relation over the 30-year interval (Figure 2A). These findings are contrary to those of Stratton et al,¹² who suggested a decrease in the slope of the CO/ $\dot{V}O_2$ relation associated with aging in a cross-sectional study. The remarkable consistency of the relation between $\dot{V}O_2$ and CO over 30 years' duration confirms the robustness of the regulatory pathways that match metabolic demand ($\dot{V}O_2$) and systemic blood flow (CO) as well as support the consistency of techniques between the evaluations.

Maximal Exercise Comparisons Before and After Training

The influence of physical activity on the age-related decrement in aerobic power has been extensively discussed.^{10,23} In the current study, with an average 17% improvement in $\dot{V}O_{2\text{max}}$ indexed to FFM after training, the group achieved a level of aerobic performance comparable to their 1966 baseline and recovered $\approx 40\%$ of the decrement demonstrated by the difference between posttraining in 1966 versus 1996 baseline.^{1,2} This observation is consistent with the estimated

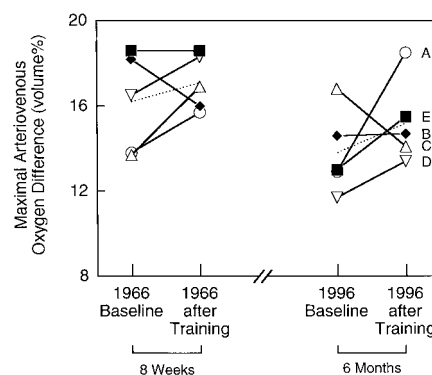


Figure 8. Maximal arteriovenous O_2 difference (vol%) before and after training in 1966 and in 1996.

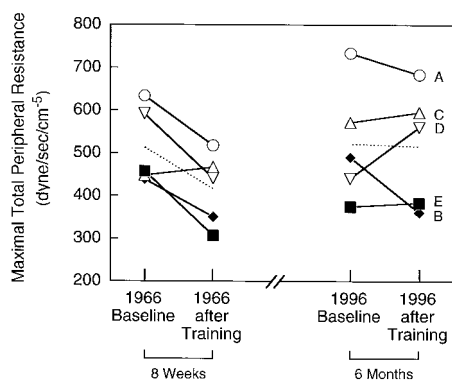


Figure 9. Maximal total peripheral resistance ($\text{dyne} \cdot \text{s}^{-1} \cdot \text{cm}^{-5}$) before and after training in 1966 and in 1996.

influence of physical activity on the age-associated decline of aerobic power from the 30-year interval baseline evaluations of these 5 men, in which a moderate correlation ($r^2=0.40$) was observed between reported habitual physical activity and measured $\dot{V}O_{2\max}$.² Similarly, in a study by Beere et al,¹⁶ older subjects recovered $\approx 30\%$ of the difference in $\dot{V}O_{2\max}$ observed at baseline between young and old cohorts following an endurance training program. These observations are also consistent with previous cross-sectional and longitudinal studies, suggesting that continued physical activity through adulthood attenuates but does not eliminate the rate of decline in aerobic power observed with aging.^{6,24,25}

Despite improvements in measures of cardiovascular fitness, the aerobic power of the subjects in the current study did not achieve the levels observed in age-matched athletes who had participated in endurance exercise throughout their adult lives²⁶ (Table 4). Whether this represents simply a difference in the duration (6 months versus many years) or intensity of training or rather a fundamental alteration of the adaptive capacity of the cardiovascular system with aging and/or deconditioning is unknown.

It is interesting to note that no improvement was observed in aerobic power after training in subject 3. Although he trained on a bicycle, he underwent cardiopulmonary testing on a treadmill. The discordance in modalities of exercise between training and testing probably explains why we were unable to demonstrate an improvement in aerobic power in this subject despite adherence to the prescribed training

TABLE 4. Results of Maximal Exercise Testing: Current Subjects Versus Previous Literature

	Dallas		Endurance Athletes, ≈ 50 y old
	Baseline	Trained	
$\dot{V}O_2$, L/min	2.9	3.3	3.6
$\dot{V}O_2$, mL/kg per minute	31	36	52
CO, L/min	21.4	21.7	26.6
HR, beats/min	181	171	171
SV, mL	121	129	156
AVDO ₂ , vol%	13.8	15.2	13.4
MAP, mm Hg	134	133	135

Previous literature is from Reference 39.

regimen. In retrospect, such a specificity of training response might have been expected because the vast majority of improvement in all other subjects appeared to be caused by peripheral rather than central mechanisms. Intriguingly, this subject was the only one with a prominent increase in CO_{\max} after training, confirming a “cross-training” effect on central versus peripheral adaptation. However, it may also suggest that with aging, the contribution of peripheral oxygen extraction to the limitations of maximal oxygen uptake may increase in magnitude.

Maximal Exercise Comparisons After Training: Current Results Versus 1966

Compared with the 1966 results, a different mechanism of adaptation to endurance training is evident in the current evaluations. Assessments of these subjects in 1966 demonstrated that the improved cardiovascular response to maximal exercise after training among younger individuals was equally mediated through an increase in CO_{\max} and maximal AVDO₂.¹ Cardiac output augmentation was achieved by a higher SV in the setting of a modest decrease in TPR at maximal effort. Similar observations have been reported in other cohorts.^{11,18,27} The current data, however, demonstrate that the improvement in aerobic power associated with training in these now middle-age men was a result of enhanced AVDO_{2max}, with no change in CO_{\max} or TPR.

Mechanisms of Adaptation

The physiological effects of endurance training have been extensively discussed.^{10,28,29} In youth and early adulthood, training results in relatively parallel improvements in central and peripheral performance.^{1,11,18} Fewer studies have evaluated the specific effects of training in middle-aged and older healthy adults with regard to central versus peripheral adaptation. Our observation that $\dot{V}O_{2\max}$ was affected primarily by AVDO_{2max} improvements with no effective change in CO_{\max} has been observed in some^{16,22,30} but not all^{12,18,19,25} prior studies. A number of plausible explanations exist to explain the observed age-associated difference in the mechanism of adaptation to endurance training.

The lack of improvement in CO_{\max} probably is caused by a number of contributing mechanisms. Aging is associated with a decline in HR_{\max} .^{3,24,31} and most studies demonstrate an additional decrement of HR_{\max} associated with training.^{1,18,27,29} In the present longitudinal study, aging appeared to magnify the reduction in HR_{\max} associated with endurance training, with a 10-beats/min decline in middle age versus no measurable change after training in youth. This prominent reduction was observed at rest and with each submaximal level of exercise as well as at maximal, arguing against it being caused by failure to achieve a true maximum heart rate after training. We speculate that the effect of an increase in “vagal tone” associated with training could be exaggerated by a reduction in responsiveness to catecholamines that has been well described with aging.^{3,6,32,33}

Maximal cardiac output was virtually unchanged after training, with a decline in HR countered by increased SV, an observation that has been made in some^{29,34} but not all prior studies.^{19,35} The ability to augment SV_{\max} to maintain CO

could be a result of an increased reliance on the Frank-Starling mechanism, increased inotropy, or both.^{6,33,36,37} It is also possible that the decreased HR_{max} rate by itself allowed for improved ventricular filling and increased SV through the Starling mechanism. Our study does not address these specific mechanisms, but previous reports suggest that aging is associated with an increased reliance on the Frank-Starling mechanism to maintain CO during maximal exercise.^{6,33,32,35,38} However, not all reports support this concept, and it remains unclear if the Frank-Starling adaptation can be sustained throughout older age.

Several plausible mechanisms have been described that could account for the improvements observed in $AVDO_{2max}$. Training has been associated with conversion of muscle fiber type from Type 2x (glycolytic) to Type 2A (oxidative)^{39,40}; increases in muscle capillary density and improvements in motor unit recruitment that increases the capillary surface area across which oxygen is exchanged^{39–41}; and increases in the efficiency of distribution of CO to exercising tissues through enhanced vasoregulation and improved motor unit recruitment.^{1,28,29,39,42} Our data do not address these specific mechanistic considerations.

Limitations

Although we attempted to administer a dose of training during the current study similar to that achieved in the 1966 study, this effort was not perfect. For example, to reduce the possible risk of injury, we eliminated the high-intensity, interval (“performance”) training component of the training prescription used in 1966. Second, we performed the training over a 6-month interval, compared with 8 weeks in 1966. Finally, in the present study, subjects achieved $\approx 10\%$ lower intensity of exercise than they did in 1966. Although the weekly duration was slightly longer, this difference resulted in a slightly lower training impulse in the present study compared with 1966.

Despite these differences, the 17% improvement in $\dot{V}O_{2max}$ indexed to FFM in the current study compares favorably with the 20% improvement achieved in the 1966 study. Moreover, a number of lines of evidence suggest that the ultimate effect of these training modifications was relatively small. First of all, performance training by itself does not substantially affect aerobic power.⁴³ Second, especially in the more untrained individuals, the majority of improvement in aerobic power in these same subjects in 1966 was achieved during the early stages of the training program, before the use of “performance” type interval training. Finally, even if the differences in training between 1966 and 1996 resulted in some diminution of the ultimate training effect, the end result was that virtually all the loss of aerobic power over 30 years of aging was restored after the training dose achieved in this study. It is very unlikely that increasing the relative intensity by 10% or adding some interval training would have dramatically increased $\dot{V}O_{2max}$ back to the posttraining level in 1966. Thus, the conclusion that similar training after 30 years reversed the aging-induced loss of aerobic power but did not return $\dot{V}O_{2max}$ to posttraining levels in youth remains valid.

The current study has other notable limitations. The limited sample size precludes meaningful statistical analysis, and the

validity of the observations should be confirmed in larger populations. The absence of a control group limits the ability to differentiate the influence of confounders, such as lifestyle, nutrition, underlying pathology, biologic/genetic differences, and others on the cardiovascular response to endurance training. Finally, the study examined the interval from youth to middle age in men only, and the results may not be generalizable to older populations or to women.

Conclusions

In summary, the age-related decline in aerobic power among these 5 middle-aged men occurring over 30 years was completely reversed by a 6-month endurance training program. However, no subject achieved the same $\dot{V}O_{2max}$ attained after intensive training as young men. The improved aerobic power after training primarily was the result of peripheral adaptation, with no effective improvement in maximal oxygen delivery.

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