line level, a 15% improvement may not have additional occupational or social benefit (8). In our study population, which was poorly conditioned at baseline, a 15% improvement could be of clinical importance in contributing to occupational and/or social function and mobility.

Although the training program demonstrated improvements in conditioning, there were no correlations with other parameters that might be directly attributed to improved conditioning, such as glucose control (10,11), weight control (10,11), serum cholesterol (12), or triglycerides, but the power to detect these changes was limited.

It may be concluded that individuals with diabetic retinopathy can be given the option of entering a cardiovascular training program. In this program, there were no untoward events associated with moderate levels of exercise training, and significant improvements in physical conditioning were noted. Some, if not all, of the differences may be due to participation in the study rather than to the effects of exercise. The role of aerobic conditioning must be further defined in future studies.

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Sperm Function and Structure and Seminal Plasma Prostanoid Concentrations in Men With IDDM

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Semen from 18 men with insulin-dependent diabetes mellitus (IDDM) aged 20–40 yr was compared with that from 15 age-matched control subjects. Although semen volume, sperm count, and spermatozoal motility were similar in the two groups, semen from diabetic men had significantly greater numbers of abnormal spermatozoa and significantly lower ability to penetrate hamster eggs. Concentrations of prostaglandins E_2, $F_{2\alpha}$, and I_2 and thromboxane A_2 were significantly elevated in the seminal plasma from semen of diabetic subjects compared with control subjects. These observations indicate the need for a careful assessment of fertility in

diabetic men, the mechanisms underlying the abnormalities in spermatozoa, and the relationship of these abnormalities to the increase in prostanoid concentrations in diabetic men. ***Diabetes Care*** **12:742–44, 1989**

Two reports have appeared about altered semen quality in diabetic men, but the magnitude of the problem cannot be inferred from these studies because the data were either collected from diabetic men already under investigation for infertility or included older men with non-insulin-dependent diabetes, in whom advancing age may have contributed to the altered sperm functions observed (1,2). We therefore studied the semen quality in young men with insulin-dependent diabetes mellitus (IDDM) via routine semen analysis and the zona-free hamster egg penetration test (HEPT). Because diabetes is associated with marked disturbances in prostanoid synthesis and metabolism (3), and prostanoids in seminal fluid may modulate the function of spermatozoa (4), we also measured the concentrations of prostaglandin (PG) E_2, $F_{2\alpha}$, and 6-oxo-$PGF_{1\alpha}$ and thromboxane B_2 (TXB_2) in the seminal plasma of diabetic patients.

RESEARCH DESIGN AND METHODS

Eighteen randomly selected IDDM male diabetic patients (mean age 31 yr, range 21–39 yr) participated in the study. Nine patients had impregnated their wives in the past. Five had a history of difficulty in impregnating their wives, the duration of infertility varying from 2 to 4.5 yr. Four had been told they had a slightly low sperm count and 2 had been on clomiphene. The wives of the 5 men had no obvious cause for their infertility. Three of these men had subsequently fathered children. The control group was comprised of 15 randomly selected healthy age-matched volunteers (mean age 29 yr, range 20–37 yr).

Patients and control subjects abstained from sexual intercourse for 3–5 days, and their semen was obtained by masturbation. A routine semen analysis was conducted for each subject. Sperm was prepared for HEPT by the method of Aitken et al. (5), and HEPT was conducted by use of the methods of Yanagimachi et al. (6). Levels of serum antisperm antibodies were assessed by the tray-agglutination technique (TAT; 7). For PG analysis, seminal plasma was centrifuged at 1400 *g* for 15 min, and the supernatants were stored at −70°C. Samples were diluted by 1×10^3, and aliquots were taken for estimation of PGE_2, $PGF_{2\alpha}$, 6-oxo-$PGF_{1\alpha}$, and TXB_2 (the stable spontaneous hydrolysates of PGI_2 and TXA_2, respectively) as previously described (8). In validation experiments, increasing concentrations added to pooled seminal plasma samples inhibited [^{3}H]PG binding in parallel with identical quantities of PGs added to distilled water. The concentrations of PGs obtained in this study were similar to those reported by other workers (4). Blood samples were collected for measurement of gonadotropins and antisperm antibodies.

RESULTS

The semen volume of the control and diabetic groups was similar (Table 1). Two of the diabetic men had azoospermia, and 1 had elevated gonadotropin levels. The median sperm density in the diabetic group was not significantly different from that of the control group. Apart from the 2 azospermic men, only 1 other subject in the diabetic group had a sperm count $<20 \times 10^6$/ml (18×10^6/ml). The percentage of motile sperm per ejaculate and their progression were also not significantly different between the two groups. However, there was a significantly higher proportion of abnormal sperm per ejaculate in the diabetic group. Among diabetic men, 7 of 16 with sperm in their ejaculate had >45% abnormal sperm forms, whereas none of the men in the control group had an abnormal sperm count >35%; the difference was statistically significant ($P < .001$). HEPT was considered abnormal if it could not be performed because of a poor sperm count or if <10% of the eggs were penetrated. Two of the diabetic men had repeated tests showing no egg penetration at all. The test was found to be abnormal in 7 of 18 diabetic men, whereas each of the men in the control group showed normal penetration. The difference was found to be statistically significant ($P < .01$). Six of 7 men with abnormal HEPT had >40% abnormal sperm forms in their ejaculate. There was no correlation between the duration of diabetes and abnormal HEPT. HEPT was abnormal in 3 of 5 men who gave a history of infertility. The other 2 had borderline (10.5 and 13.3%) test results. Both had ultimately achieved a pregnancy with their partners. Of

TABLE 1
Comparison of sperm function and structure and seminal plasma prostanoid concentrations in IDDM and nondiabetic control men

Test	Control	IDDM
Semen volume (ml; mean)	2.6 (1.5–9.8)	2.8 (1.7–4.5)*
Sperm count (per ml × 10^6; median)	64.5 (1–190)	88.6 (33–230)*
Abnormal sperm per ejaculate (%; mean ± SD)	27 ± 4	42.9 ± 9.98†
Prostaglandins (μg/ml; mean ± SE)		
PGE_2	22 ± 2.5	41 ± 5‡
$PGF_{2\alpha}$	4 ± 0.4	7 ± 1.3‡
6-oxo-$PGF_{1\alpha}$	1.5 ± 0.2	4.1 ± 0.5‡
Thromboxane B_2	0.0032 ± 0.001	0.008 ± 0.001‡

Ranges are in parentheses. IDDM, insulin-dependent diabetes mellitus.
*NS, †$P < .01$, ‡$P < .001$.

the 5 subfertile men, 4 had >40% abnormal sperm forms in their ejaculate, and the 5th was azoospermic. One person in each group had a significant concentration of serum antisperm antibodies. The concentrations of all PGs investigated were significantly greater in diabetic men than in control subjects, but there was no significant correlation between PG levels and either structural abnormalities of spermatozoa or abnormal HEPT.

DISCUSSION

The significantly higher proportion of abnormal sperm forms in the semen of young diabetic men reported herein concurs with previous reports (1,2). However, our study did not suffer from the drawbacks of the previous studies, which reported results from infertile men who happened to be diabetic (1) or included older diabetic patients in whom advancing age may have altered semen characteristics (2). Our findings are also consistent with testicular abnormalities found in diabetic men, i.e., increases in tubular tunica propria thickness and interstitial tissue volume, a reduction of the internal volume of the tubules, and a general hypospermatogenesis with partial arrest in sperm maturation (9).

Although the precise role of PGs in sperm function is unclear, a positive relationship between seminal PG content and fertility has been established (4). Elevated seminal plasma PG concentrations have been associated with oligospermia and decreased sperm motility (4), but we did not find these sperm defects in the diabetic men investigated. Furthermore, it is unlikely that elevated PG accounts for diminished ability of diabetic sperm to penetrate hamster eggs because this process is actually enhanced by PGE_1 and PGE_2 (4). However, the possibility that elevated seminal PG is associated with increased abnormal sperm forms warrants further investigation.

The adverse effects of diabetes on male sexual dysfunction has largely focused on the prevalence of erectile dysfunction and retrograde ejaculation (1,2). The incidence of impotence reported was ~50% in a group of patients with an average age of 50 yr. However, erectile and ejaculatory problems should not alter fertility potential because most of these men would have completed their families by the time the problems occurred. Unfortunately, no epidemiological information is available on the reproductive potential of the younger IDDM male. Nonetheless, given the high incidence of abnormal sperm structure and function in young diabetic men in whom the creation of a family is of importance, the possibility of diminished reproductive potential via sperm dysfunction warrants further consideration and research.

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