Exercise as a Risk Factor for Infertility with Ovulatory Dysfunction

BEVERLY B. GREEN, MD, MPH, JANET R. DALING, PHD, NOEL S. WEISS, MD, DRPH, JONATHAN M. LIFF, PHD, AND THOMAS KOEPSELL, MD, MPH

Abstract: To examine the relation of regular vigorous exercise to ovulatory infertility, we interviewed 346 infertile women, in whom there was evidence of ovulatory failure, regarding their exercise patterns during the year preceding their unsuccessful effort to conceive. Their responses were compared with similar exercise histories in women who had successfully conceived at the time the infertile women started trying to become pregnant. Vigorous exercise for an hour or more per day was reported more commonly in nulligravid cases (n = 187) than by their primiparous controls. The difference was particularly great in the subgroup of cases without additional evidence of tubal dysfunction (relative risk = 6.2, 90% confidence interval = 1.0 – 39.8). This association was not seen among infertile women who had previously been pregnant. Vigorous exercise for an average of less than one hour per day was not associated with either primary or secondary infertility. (*Am J Public Health* 1986; 76:1432–1436.)

Introduction

There is accumulating evidence that regular strenuous exercise alters menstrual function.[1] The frequency of ammenorrhea or oligomenorrhea among women participating in a variety of strenuous sports varies from 2 to 51 per cent (depending on the definition of these terms), as opposed to 2 to 5 per cent of other women.[2] In a prospective study of women with previously normal ovulation and luteal function, 87 per cent experienced abnormalities of these reproductive functions while engaging in a strenous exercise program.[3] From data collected in our study of infertile women in King County, Washington, we attempted to evaluate whether women who participate regularly in vigorous sports are subsequently at higher risk of infertility.

Methods

This analysis is part of a larger study in which 20- to 39-year old female residents of King County, Washington whose first medical evaluation for infertility occurred during the years 1979–81. More detailed methods for case and control selection are presented elsewhere.[4]

For the purpose of the present analysis, we chose the subgroup of women defined as being infertile (those who did not conceive despite trying for at least one year) in whom an ovulatory abnormality was present (Table 1). The latter assessment, made by the patient's physician, was based upon a history of oligomenorrhea (defined here as menstrual cycles 35 days or greater), ammenorrhea, or an abnormal basal body temperature graph showing either a monophasic pattern or luteal phase defect. If the menstrual history and basal body temperature data conflicted, the basal body temperature criterion was used. Three hundred and eighty women were judged possibly to have an abnormality of ovulation as the basis for their infertility (39 per cent of all infertile subjects). A number of these women also had other abnormalities that could have been responsible for infertility, such as tubal disease, endometriosis, or oligospermia of the partner.

From the Department of Family Medicine, University of Washington, Department of Epidemiology, U-WA School of Public Health and Community Medicine, and the Division of Public Health Sciences, Fred Hutchinson Cancer Research Center (in Seattle), and the Department of Community Health, Emory University School of Medicine (Atlanta). Address reprint requests to Beverly B. Green, MD, MPH, Fred Hutchinson Cancer Research Center, Division of Public Health Sciences (W 108), 1124 Columbia Street, Seattle, WA 98104. This paper, submitted to the Journal December 6, 1985, was revised and accepted for publication May 27, 1986.

There were 206 women who had not previously conceived a child ("primary" ovulatory infertility) and 174 women who had previously conceived ("secondary" ovulatory infertility). As a basis for comparison, we used Washington State Vital Records to identify married King County residents who gave birth during the calendar year following the one in which the case started trying to become pregnant. The "reference date" is defined as the month and the year that the case started trying to conceive and the control successfully conceived. From the information contained in the birth record, each control was matched to a case by race, census tract of residence, and age (within five-year groups). Four controls were identified for each case (in order to have back-up controls in the event a control could not be reached or refused to be interviewed). An attempt was made to match on gravidity as well. While this proved successful in cases with primary infertility and previously nulligravid controls, in approximately 10 per cent of the birth certificates the information on gravidity did not agree with that obtained in the interview. Thus, secondary infertility cases with an ovulatory abnormality were compared with all controls who had previously conceived.

In the questionnaire, exercise histories were obtained retrospectively from the interview date over a five-year period, asking the women in what regular sports and exercise they had participated on a regular basis and how frequently and for what time duration these activities were performed. We included in our analysis exercise that was performed in the year preceding the conception (controls) or the initiation of the unsuccessful attempt to conceive (cases). As some of the women had been interviewed several years after their "reference date," data on exercise prior to the reference date were missing on such women. These women were excluded from further analysis. The excluded cases were equally distributed between primary infertility cases and controls (7 per cent) and secondary infertility cases and controls (9 per cent). Of the remaining women, each had zero to three activities listed for this time period.

Each woman was then categorized into one of three exercise groups according to the average minutes per day she exercised, adding together all the time spent on these three activities. These categories included no regular exercise (non-exercisers or women who exercised less than an average of 7 minutes per day), light to moderately heavy exercisers (women whose average exercise time per day was between 7–59 minutes per day), and extremely heavy exercisers (women who exercised 60 minutes or more per day). These categories were repeated for time spent doing vigorous

TABLE 1—Selection of Cases and Controls for Infertility Study

	Primary Infertility		Secondary Infertility	
	Cases	Controls*	Cases	Controls**
All diagnoses and controls[a]	544	536	461	473
Ovulatory abnormalities diagnosed[b]	206	—	174	—
Subjects excluded based on				
data missing on exercise	14	14	12	45
data missing on covariates	5	5	3	9
Cases with ovulatory abnormalities and controls analyzed[b]	187	187	159	419
Number of cases with ovulatory infertility and controls:				
Excluding those with an additional tubal diagnosis	137	137	128	419
Excluding those with any other additional diagnosis	94	94	91	419

*Controls for primary infertility cases were matched so that exclusion of a case or control subject necessitated removal of the matched case or control subject.

**Controls for secondary infertility cases were not matched.

[a]All cases, irrespective of diagnosis, e.g., ovulatory, tubal, cervical, endometriosis, male factor, or other "type" of infertility.

[b]Subjects could have other possible reasons for their infertility in addition to their ovulatory abnormality.

exercise only. Vigorous exercise was defined as aerobic activities that require .01 KCAL/min/day or more to perform (roughly 6 KCAL/minute for an average-weight woman). Examples of vigorous activities include running, bicycling, swimming, aerobic dancing, tennis, and downhill skiing. Activities of lower caloric expenditure include walking, gardening, horseback riding, golf, and bowling. Average KCAL/day/kg for all exercise and vigorous exercise only for each woman was calculated using McArdle's Appendix,[5] which lists average caloric expenditures per kilogram for specific physical activities for women. Calculated caloric expenditure correlated very closely with average exercise time (r = 0.99) for both vigorous and nonvigorous exercise. For simplicity, only exercise time is presented here. Women who exercised vigorously an average of 60 minutes or more per day most commonly engaged in running, aerobics, or dancing, but bicycling, soccer, rowing, tennis, and skiing were reported as well.

In addition to the matching variables, we also analyzed other variables that might be related to either exercise or infertility, including socioeconomic variables (level of income, education, and social class of the occupation of respondents and their spouses), past birth control use, number of past sexual partners, past drug and smoking habits, and history of sexually transmitted diseases. Other covariates analyzed included body weight at time of successful or failed conception, weight relative to height indexes, and per cent weight under or over ideal body weight (Metropolitan Life Insurance tables[6]). We also looked at exertion typical of the respondent's job (as listed in the appendix of the Dictionary of Occupational Titles[7]) and tested these categories for any confounding effects on the relative risk of exercise and infertility.

The association between vigorous exercise and ovulatory infertility was analyzed using a conditional logistic regression technique[8] that estimates odds ratios. The relative

TABLE 2—Characteristics of the Infertility Study Population

Variables	Primary Infertility Cases No. (%)	Primary Infertility Controls No. (%)	Secondary Infertility Cases No. (%)	Secondary Infertility Controls No. (%)
Age at Reference Date (years)				
<25	67 (32)	69 (33)	46 (26)	98 (21)
25–29	100 (49)	98 (48)	70 (40)	214 (45)
>30	39 (19)	39 (19)	58 (34)	161 (34)
Annual Family Income*				
<$15,000	22 (11)	44 (21)	18 (10)	74 (16)
$15,000–$30,000	88 (43)	96 (47)	90 (52)	248 (52)
≥$30,000	95 (46)	65 (32)	65 (38)	149 (32)
No. of Marriages*				
1	163 (80)	170 (85)	114 (68)	370 (79)
≥2	40 (20)	29 (15)	56 (32)	97 (21)
No. of Past Sexual Partners (Lifetime)*				
1–4	143 (70)	163 (79)	116 (67)	341 (72)
5+	60 (30)	43 (21)	58 (33)	132 (28)
Parity Prior to Reference Date				
0	206 (100)	206 (100)	74 (43)	130 (27)
≥1	0	0	100 (57)	343 (73)
Per Cent of Ideal Weight† at Reference Date				
≤85%	17 (8)	5 (2)	10 (6)	18 (4)
86%–119%	165 (80)	183 (89)	135 (77)	379 (80)
≥120%	24 (12)	18 (9)	29 (17)	75 (16)
Average Min/Day Exercise (All Exercise)				
Non-exercise	133 (67)	120 (60)	112 (69)	306 (72)
<60 Min/Day	51 (25)	70 (35)	45 (28)	108 (25)
≥60 Min/Day	15 (8)	9 (5)	5 (3)	14 (3)
(Missing Information)††	(7)	(7)	(12)	(45)

*Some women refused to answer these questions.

†Information on weight in one control for the secondary infertility cases was not obtained.

‡Information on exercise is missing in these women (see text).

TABLE 3—Vigorous Exercise Time in Women with Primary Infertility and Controls

A) All Primary Cases with an Ovulatory Abnormality

	Cases		Controls		Relative Risk[a]	90% Confidence Interval
	%	(No.)	%	(No.)		
Average min/day Vigorous Exercise						
Non-exercisers	71	(133)	65	(121)	1	
<60 min/day	24	(45)	33	(62)	0.6	0.4– 0.9
≥60 min/day	5	(9)	2	(4)	1.9	0.6– 5.1

B) Excluding Cases with Evidence of Tubal Dysfunction

	Cases		Controls		Relative Risk[b]	90% Confidence Interval
	%	(No.)	%	(No.)		
Average min/day Vigorous Exercise						
Non-exercisers	69	(94)	66	(91)	1	
<60 min/day	26	(36)	33	(45)	0.7	0.4– 1.2
≥60 min/day	5	(7)	1	(1)	6.2	1.0–39.8

[a]Risk relative to that in women who did not exercise, adjusting for matching variables, income, and number of past sexual partners.
[b]Risk relative to that in women who did not exercise, adjusting matching variables, income, and deviance from ideal weight.

TABLE 4—Vigorous Exercise Time on Women with Secondary Ovulatory Infertility

A) All Secondary Ovulatory Cases and Controls

	Cases		Controls		Relative Risk[a]	90% Confidence Interval
	%	(No.)	%	(No.)		
Average min/day Vigorous Exercise						
Non-exercisers	74	(117)	78	(327)	1	
<60 min/day	25	(40)	21	(87)	1.2	0.8–1.8
≥60 min/day	1	(2)	1	(5)	0.9	0.2–3.6

B) Excluding Cases with Evidence of Tubal Infertility

	Cases		Controls		Relative Risk[b]	90% Confidence Interval
	%	(No.)	%	(No.)		
Average min/day Vigorous Exercise						
Non-exercisers	73	(93)	78	(327)	1	
<60 min/day	26	(33)	31	(87)	1.3	0.8–1.9
≥60 min/day	1	(2)	1	(5)	1.3	0.3–5.2

[a]Risk relative to that in women who did not exercise, adjusting for age group, race, census tract of residence, reference year, parity, and times married.
[b]Risk relative to that in women who did not exercise, adjusting for age group, race, census tract of residence, reference year, and parity.

risk of primary ovulatory infertility in vigorous exercisers was analyzed, controlling for confounding variables, using conditional logistic regression. The relative risk of secondary ovulatory infertility in vigorous exercisers was analyzed using an unconditional logistic regression, controlling for both the variables matched for in the primary infertility case and control group (as previously listed) and confounding variables simultaneously.

Results

Table 2 compares some characteristics of cases and controls. Variables that were found to have potential confounding effects on the relation of exercise to infertility included family income, past number of marriages and sexual partners, past parity, and per cent of ideal weight. Cases and controls were similar with respect to age, smoking history, and activity level of and social class of their regular occupation at the time of the reference date. Among nulligravid women with ovulatory abnormalities, 8 per cent exercised 60 minutes or more per day, as compared with 5 per cent of their controls (relative risk = 1.7, 90% confidence interval 0.8 – 3.5). In secondary infertility, the same percentage of cases and their controls (3 per cent) exercised 60 minutes or more per day (relative risk = 1.0, 90% confidence interval 0.4 – 2.3).

Five per cent of the primary cases and 2 per cent of the controls engaged in vigorous exercise 60 minutes or more per day (Table 3a). The relative risk associated with vigorous exercise was 1.9 (90% confidence interval = 0.6 – 5.1), adjusting for both the matching variables and the confounding effects of income and number of past sexual partners.

Twenty-seven per cent of the primary cases and 19 per cent of the secondary cases had a tubal condition present as well. When we reanalyzed the distribution of vigorous exercisers excluding women who had a tubal abnormality (Table 3b), we found an increased risk in women who exercised vigorously 60 minutes or more per day (relative risk = 6.2, 90% confidence interval 1.0 – 39.8). In the condition logistic model from which this relative risk was obtained, we controlled for the effects of income and the woman's per cent deviance from her ideal weight (categories as previously defined). If per cent ideal weight was not controlled, the relative risk in extreme exercisers was little changed (relative risk = 5.8, 90% confidence interval of 0.9 – 35.8).

If women with all other suspected causes of infertility were excluded, leaving women with an ovulatory abnormality only (n = 94), the relative risk associated with vigorous exercise for 60 minutes or more per day decreased slightly to 4.7 (90% confidence interval of 0.8 – 28.0). Many of these women, however, received only an incomplete evaluation for other possible causes of infertility.

Table 4a compares the vigorous exercise time in cases with secondary infertility and an ovulatory abnormality with that in controls. There is a lack of association of vigorous exercise time of 60 minutes or more per day and infertility on these women (relative risk = 0.9, 90% confidence interval 0.2 – 3.6). This same lack of association was present when cases with tubal abnormalities were excluded (Table 4b) and when women with any suspected cause for their infertility other than an ovulatory abnormality were excluded.

Discussion

This study had several limitations that may have biased the results. First, although most of the women we identified who sought care for infertility in King County between 1979 and 1981 took part in the study, we made no effort to identify infertile women who did not seek care. Women in this latter category could represent a substantial proportion of those who are infertile, since the cost of a clinical evaluation of infertility is high and generally not covered by medical insurance. Selection as a control was not conditional on this type of clinical evaluation. Thus, if vigorous exercise of long duration was either less or more common among the unidentified cases, selection bias could have taken place. The similar number of cases and controls engaging in at least some exercise argues against a large degree of bias.

Second, the validity and reliability of the exercise information on our subjects was not documented. Similar questionnaires (such as the Minnesota Time Activity Questionnaire[9]) have been found to be reliable in middle-aged men.[9] Increasing levels of vigorous activity as reported in the questionnaire have been correlated with increased exercise treadmill performance.[9] The validity of this type of questionnaire, however, has not been verified in young women. Women may under- or overestimate their exercise time, resulting in misclassification of exercise intensity levels. In addition, some of the cases and controls were interviewed several years after their reference year. This delay resulted in missing exercise data for some cases and controls. In addition, some women may have not have remembered precisely the types, times, and years of specific physical activities, resulting in misclassification of exercise exposure. There is no reason, however, to suspect that the cases would have answered differently from controls, and missing data were equally distributed between cases and controls. In addition, cases and controls had a similar distribution of the date of their interview year relative to their reference year, and reference year was either matched on or controlled for in the final logistic models.

Third, cases were classified as having an ovulatory abnormality based on either having abnormal menses or an abnormal basal body temperature graph as diagnosed by their physician. These criteria are inexact measures of ovulatory function. More precise diagnostic tests exist[10] (such as endometrial biopsies and post-ovulatory progesterone levels), but these tests were less frequently performed in our study subjects. To complicate matters further, many infertile women with evidence of an abnormality of ovulation also had evidence of other abnormalities that could have been responsible for their infertility. One possible way of reducing this source of misclassification would have been to confine the analysis to women with ovulatory dysfunction who had no other explanation for their infertility. In this group of women, however, many of the diagnostic tests for the other causes of infertility had not been performed. When we excluded infertile women with other abnormalities (first those with tubal pathology and then those with any other condition), we continued to find an elevated risk of primary infertilty associated only with vigorous exercise for one hour or more per day. Of those women with causes for their infertility other than ovulatory dysfunction, those with tubal pathology were the largest subgroup. Risk factors for tubal infertility have been described previously.[4] These defined risk factors could potentially obscure other risk factors associated with reproductive dysfunction.

The results of this study consistently showed a lack of association between infertility with ovulatory abnormalities and less than vigorous exercise or vigorous exercise for less than 60 minutes or more per day. Women who had previously been pregnant were not at increased risk of infertility at any duration of vigorous exercise. There was evidence, however, of an increased risk of infertility in nulligravid women who reported exercising vigorously 60 minutes or more per day, particularly among the case group without tubal damage or other explanations for their infertility.

Menstrual irregularities are present in an abnormally high percentage of female runners,[11] ballet dancers,[12] and in participants in a variety of other vigorous sports.[13] The menstrual dysfunction described in these women includes hormonal changes, luteal phase changes, and annovulation.[14,15] There is little information on the relation of exercise-induced menstrual irregularities to infertility. Shangold and Levene reported that 10 per cent of 394 runners had a history of past or present infertility.[16] This proportion is similar to estimates of the frequency of infertility in the general population.[17] The majority of women in Shangold and Levene's study, however, were using birth control methods at some time and may not have tested their ability to conceive. If so, the result would be an underestimation of the frequency of infertility among the marathon runners.

The reversibility of exercise-induced menstrual changes has been documented.[3,18] Weight, age, age at menarche, and gravidity may be important in determining which women are more susceptible to exercise-induced menstrual changes.[1,3] In the present study, vigorous exercise in previously pregnant women was not a risk for ovulatory infertility.

There is considerable debate about the relation of weight and exercise to menstrual dysfunction.[19,20] In our study, having a weight for height 85 per cent or less than an ideal was associated with an increased risk of infertility with ovulatory dysfunction. Controlling for weight did not materially alter the risk of extreme exercise and primary infertility. Thus, exercise appears to exert its effect through a means independent of its ability to produce weight loss. There were too few extreme exercisers to evaluate whether the joint effect of vigorous exercise and being underweight on the occurrence of infertility was more than the independent effects of each alone.

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USA for Africa Medical Task Force Announces $1.5 Million in Grants

The Medical Task Force of United Support of Artists for Africa (USA for Africa) has announced grants totaling $1,439,932 for 11 African-related projects. The funds for these grants were derived from the hit recording, "We Are The World," and related projects, which had raised approximately $48,750,000 as of September 1, 1986. The USAFA-funded projects are:

- Provision of emergency medical supplies through International Committee of the Red Cross (ICRC) for Eritrea and Tigrah, Northern Ethiopia, $67,720.
- Emergency medical supplies (ICRC Emergency Project) to Southern Sudan, $73,080.
- Emergency medical and famine relief project to be administered by the Canadian Physicians for African Refugees (CPAR) in Semada, Woreda, Ethiopia, $160,300.
- Emergency medical kits of essential drugs for Ethiopia, through United Nations Children's Fund (UNICEF), $290,704.
- Emergency medical assistance in western Sudan including vaccination for children, emergency health care, and nutritional supplement for 60,000 Chad refugees, through United Nations High Commission for Refugees (UNHCR), $110,880.
- USA for Africa Health Scholars program at Louisiana State University for young scientists from developing African nations to study for advanced degrees in public health and human nutrition, $100,000.
- Program for the control of nutritional blindness and trachoma among children in Mauritania, through Helen Keller International, $273,490.
- Vaccination programs in Southern White Nile Province and in North Kordofan Province, Sudan, through Concern Sudan, $51,549.
- Program for training of families and communities in Mali in protective health behavior, through Save the Children Federation, $253,209.
- Reconstruction of the sole health care clinic in the Beboto region of Chad, through World Concern, $5,000.
- Program for training African medical personnel to improve the health status in two areas of Burkina Faso, through Unitarian Universalist Service Committee, $54,000.

For additional information, contact Irwin Redlener, MD, Chairman, Medical Task Force, USA for Africa, 100 East 85th Street, New York, NY 10028. "We feel that these programs are effective in covering a wide range of medical needs in Africa," Dr. Redlener said. "Our task is not only to alleviate the current medical crisis that exists in many of the African regions, but to develop medical self-sufficiency for the population there."

Members of the USAFA Medical Task Force include: Dr. Redlener, J. Larry Brown, PhD, Nicholas Cunningham, MD, DrPH, David Fraser, MD, H. Jack Geiger, MD, Rose Gibbs, MD, Lloyd Greig, MD, Robert Haggerty, MD, Steven C. Joseph, MD, MPH, Jennifer Leaning, MD, George Lythcott, MD, Marshall McBean, MD, Russell Morgan, DrPH, Victor W. Sidel, MD, and Joe Wray, MD.