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ORAL CONTRACEPTIVES AND EXERCISE[1]

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Abstract. Twelve college women, 5 naturally cycling and 7 on oral contraceptives, participated in a study to determine if oral contraceptives have an effect on selected hematologic and metabolic variables. The women worked at 2 workloads on a bicycle ergometer: 50% and 90% of their maximal aerobic capacity during 3 phases of the menstrual cycle, post mensus, ovulation, and mid-luteal. Within group differences were examined to determine if one time of the month was more suitable for doing submaximal or near maximal work, and between group differences were examined to determine the effects of oral contraceptives. Within the 2 groups, there were no significant differences for any variables. Between group differences were associated with higher heart rate and ventilation values for the women on oral contraceptives when the workloads were near maximal.

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Physiological variations associated with the naturally cycling female menstrual cycle have been well documented in the literature. Performance, mental outlook, and blood variables have been extensively studied (Curtis-Prior *et al* 1974, Dalton 1960, Gamberale *et al* 1975, Garlick and Bernauer, Doolittle and Engebretsen 1972), but the results are not entirely clear since some authors have reported changes in blood and metabolic factors while others maintain that physiological variations during the menstrual cycle are slight, if any at all.

Lacking in the literature are any values for oxygen consumption ($\dot{V}O_2$), ventilation ($\dot{V}E$), and heart rate during steady state or near maximal levels of exercise in women taking oral contraceptives. The present study compares the relative metabolic, ventilatory, and blood factors of 12 women to determine how these factors were affected in subjects using oral contraceptives.

METHODS AND MATERIALS

Twelve college women (ages 20–25) gave their informed consent and volunteered for this study. All were given examinations by their family physician, who had been previously informed regarding the nature of the study. The subjects were in good health, and none was participating in endurance sports. Vital data for the 2 groups appear in table 1.

Each subject reported to the laboratory for an explanation of the study, familiarization with the bicycle ergometer and mouthpiece (Warren E. Collins Triple J), and to ride several workloads of low intensity (>25% of maximal arobic capacity). On the second visit to the laboratory, 2 more rides were carried out with the second ride calculated to approximate the subject's maximal aerobic capacity. If the subject was able to complete that ride, she returned on another day for another maximal effort. When the subject could no longer maintain the pedal frequency (60 revolutions per minute) or when values for $\dot{V}O_2$ were within 1% for two rides, maximal aerobic power was assumed to have been achieved. During the last minute of each ride, values for $\dot{V}O_2$, heart rate, and $\dot{V}E$ were determined. Inspired volumes were calculated using a Parkinson Cowan CD 4 dry gas meter, and expired volumes were collected in Douglas bags. Oxygen was analyzed in a Beckman E2 oxygen analyzer, and carbon dioxide in a Beckman-Spinco LB-1 CO_2 analyzer. Both were carefully calibrated with analyzed gases. Heart rate was recorded on a Hewlett Packard electrocardiograph Model 1500A.

The subjects reported to the laboratory 3 times a month for 3 consecutive months or until 3 months of data were completed. The 3 monthly visits corresponded to their particular monthly cycle and coincided to the following: termination of mensus, ovulation, and mid-luteal phases. The naturally cycling women used a rise in oral temperature as an indication of ovulation. In the women taking the contraceptives, the ovulatory phase was estimated as the mid-point in the cycle. In both groups,

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mid-luteal was estimated as a day midway between ovulation and the onset of the next mensus. All of the women on the pill had regular mensus and mid-luteal estimations were made with relative confidence. Each subject was in almost daily contact with the staff, and the day immediately following mensus or following a temperature rise in the naturally cycling women, the subject reported to the laboratory. All rides were carried out at the same time of day for each phase of the menstrual cycle.

During a typical experimental ride, subjects adhered to the following procedures. In each group, 4 subjects consented to have blood drawn, and the first procedure was to withdraw 10 ml of blood from an anticubital vein. While seated on the bicycle ergometer, the subject's resting heart rate and blood pressure (BP) were recorded. Based on the preliminary series of rides, two workloads representing approximately 50% and 90% of the subject's maximal aerobic capacity were selected, and each subject rode these two workloads for 5 minutes with 10 minutes of rest between rides. The previously mentioned metabolic and ventilatory variables were measured during the last minute of each of these rides.

The red blood count (RBC), white blood count (WBC), hemoglobin (Hb), hematocrit (Hct), and red blood cell indices were determined on a Coulter Counter (Model S). Blood urea nitrogen (BUN), glucose, sodium (Na^+), potassium (K^+), and chloride (Cl^-) were determined on a Technicon (SMA 6/60). The serum creatine phosphokinase (CPK) was analyzed on a Gilford 300N Spectrophotometer and Automatic Enzyme Analyzer, and cholesterol was determined manually utilizing Hycel Cholesterol Reagent. A differential leukocyte count was determined from a blood smear made at the time of venipuncture. The smear was stained with Wright's stain, and 100 white cells were differentially counted and converted to a percentage of the total leukocyte count.

All statistical procedures for the between group comparisons were calculated using a nested analysis of variance model, and within group comparisons were made using a one-way analysis of variance.

RESULTS AND DISCUSSION

Initial subjective observations indicated that the women rode all the rides with relative ease, and none complained that any specific time of the month was more or less difficult. This important subjective evaluation has a great deal to do with the outcome of such a study, for any psychological factors imposed on the subjects could easily affect heart rate, $\dot{V}_E$, and BP.

Between group comparisons. While women on the oral contraceptives were seated on the bicycle, their resting heart rate was significantly higher ($P<.01$) than normally cycling women (table 1). As expected, there were no significant differences between the 2 groups for $\dot{V}O_2$ at the 50% maximal aerobic capacity level, but heart rate at submaximal load was significantly higher ($P<.01$) for women using oral contraceptives (fig. 1). At the near maximal levels of aerobic capacity, the naturally cycling women were working at 89% of maximal, and the women on oral contraceptives were working at 86% of maximal. The workloads were 158 watts and 154 watts respectively. Even though the women on oral contraceptives were working at a slightly lower percentage of their maximal aerobic capacity, both their heart rate and V_E

TABLE 1

Vital data for female subjects taking contraceptives as compared to naturally cycling females.

Age	Ht(cm)	Wt(Kg)	max $\dot{V}O_2$ (ml/Kg-min)	Resting Ht rate	Pill type
On Contraceptives (n = 7)					
20	167.5	51.2	32.38	105.82	Ortho Novum 1/50 Ortho
21	164.0	66.5	29.07	99.76	Ovulen 28 Searle
20	175.2	60.7	34.93	94.96	Demulen 21 Searle
20	164.0	52.0	35.56	83.53	Ovral Wyeth
25	165.0	60.2	27.16	100.13	Ortho Novum 1/50 Ortho
23	166.0	73.1	27.09	78.62	Loestrin 1.5/30 Parke-Davis
20	164.9	59.9	30.30	71.09	Loestrin 28 Parke-Davis
Mean 21±2**	166.6±4*	60.5±7.7*	30.9±2.5*	90.6±3**	
Natural Cycle (n = 5)					
Mean 19±0.6	163.7±5	60.9±11	32.9±2.4	80.7±12	

*Not significant, mean±SD.
**$P<.01$.

TABLE 2

Summary of comparative blood data in females taking contraceptives and natural cycling females.

	PM	OV	ML
Contraceptive (n = 7)			
WBC/mm³ x 10³	5.50±1.8*	6.47±0.7	7.17±1.3
RBC/mm³ x 10⁶	4.65±0.2	4.54±0.2	4.46±0.2
HB gm/dl	13.96±0.5	13.72±0.8	13.49±1.0
Hct vol %	40.83±2.1	39.80±2.2	39.00±2.7
Natural Cycle (n = 5)			
WBC/mm³ x 10³	6.64±0.9	7.04±0.8	7.36±0.8
RBC/mm³ x 10⁶	4.64±0.4	4.52±0.3	4.57±0.2
Hb gm/dl	13.60±0.8	13.36±0.8	13.50±0.7
Hct vol %	40.24±1.1	38.40±1.4	39.98±1.2

*Mean ± Standard Deviation, no significant differences between groups. PM = post menses. OV = ovulation, ML = midleuteal.

were significantly higher ($P < .01$) than those of the naturally cycling women under the same exercise conditions (figs. 2 and 3).

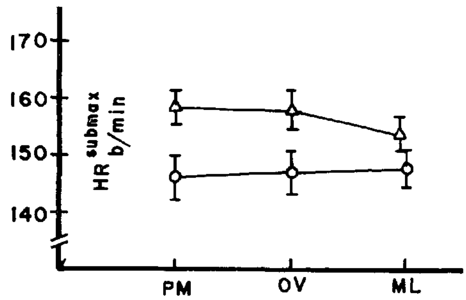

FIGURE 1. Heart rate at approximately 50% of work load (beats/min) as a function of time within the monthly cycle. PM = post menses, OV = ovulation, ML = mid-leuteal. Cumulative mean ± SE from subjects over a 3 month period. Normally cycling women (0) n = 5, women on oral contraceptives (△) n = 7.

There were no significant differences for any of the blood variables studied between these 2 groups of women (See table 2).

Within group comparisons for both the naturally cycling women and the women on oral contraceptives showed no statistical differences for any of the blood or metabolic variables. One obvious trend in the blood data was the rise in the WBC's from post mensus to mid-luteal. This trend in the WBC data is consistent with the work of Fish and Friedman (1973), who showed a similar rise. Their proposed mechanism for this response is associated with the steroid hormones stimulating the bone marrow for increased production.

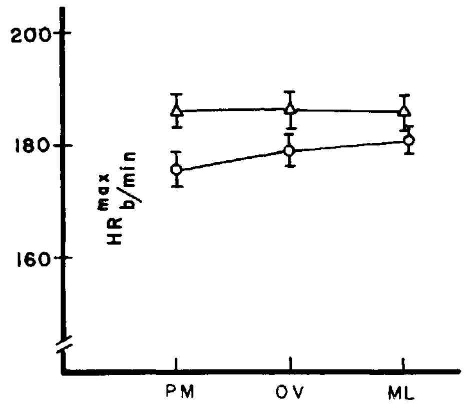

FIGURE 2. Heart rate at maximal work load (beats/min) as a function of time within the monthly cycle. Cumulative mean ± SE over a 3 month period with normally cycling women (0) n = 5 riding at 89% of maximal aerobic capacity and women on oral contraceptives (△) n = 7 working at 86% of maximal aerobic capacity.

The between group metabolic data demonstrate some important physiological differences. The women on the oral contraceptives had higher values for heart rate and $\dot{V}_E$ at a lower percentage of maximal workloads than the women who were naturally cycling. These values indicate that the women on oral contraceptives have somewhat reduced cardiac efficiency and are ventilating more to carry out a given amount of work when compared to the naturally cycling women. Such differences were also apparent for their heart rate at the 50% rides.

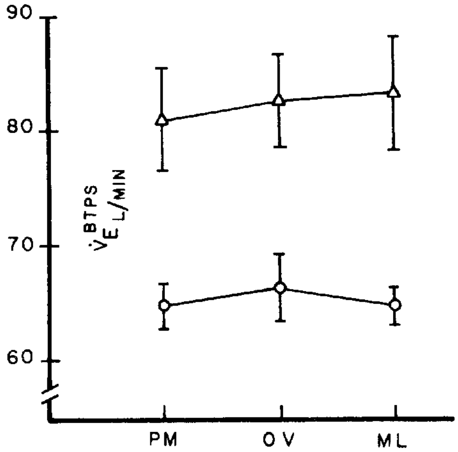

FIGURE 3. Minute ventilation ±SE (ℓ/min) as a function of time within a monthly cycle. PM=post menses, OV=ovulation, ML=midleuteal. Cumulative means over a 3 month period with normally cycling women (0) n=5 riding at 86% of maximal aerobic capacity, and women on oral contraceptives (△) n=7 working at 86% of maximal aerobic acpacity. (BTPS =body temperature, pressure, saturated.)

Possible explanations as to why values for heart rate at rest and exercise were higher in the women on oral contraceptives could include: 1. elevation of plasma cortisol (Layne *et al* 1962), 2. total serum thyroxin (Mishell *et al* 1969), 3. an increase in blood viscosity (Aronson *et al* 1971). Cortisol and especially thyroxin are well known to increase heart rate over normal values, but thyroxin is calorigenic and increases metabolic rate. No evidence exists of such an increase in any of the $\dot{V}O_2$ data in our study.

Aronson (1971) found that a rise in blood viscosity occured in women taking oral contraceptives but that the rise in viscosity was also accompanied by an increase in the hematocrit. An increase in blood viscosity could be an important consideration in explaining the reduced cardiac efficiency in the women on oral contraceptives, but this explanation is not supported by our data because we found little difference in hematocrit level between the 2 groups. Blood viscocity is also a function of plasma protein concentration, particularly fibrinogen and globulin. Pindyck (1970) found an elevation of cyrofibrinogens in women taking oral contraceptives while Mendenhall (1970) found an increase in macroglobulins. Both findings suggest protein as a contributing factor for an increase in blood viscosity and an increase in the work of the heart.

Several limitations are inherent in our study, particularly the small number of subjects used as well as limited sampling within one menstrual cycle. We attempted to reduce the statistical difficulties of small sample size by replicating the experimental design over a period of 3 months. As far as sampling times within the menstrual cycle were concerned, our collection times certainly were associated with known variations in plasma hormone levels and, as such, meet the purposes of the experimental design.

Within these 2 groups of women we found little metabolic or hematologic variation. It is fully understood that performance during menstrual flow might be uncomfortable, and there may be some psychological factors which could affect the ability to do heavy work or extended periods of steady state work (Erdelyi 1962, Wearing *et al* 1972). Other than during menstruation, we found no one time of the month more or less conducive for performing steady state or maximal levels of work. It is concluded that women taking oral contraceptives have a tendency for increased heart rate and $\dot{V}_E$ values at near maximal levels of work capacity and increased heart rate at approximately 50% of aerobic capacity when compared to women who are naturally cycling.

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