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Effects of human pregnancy and advancing gestation on respiratory discomfort during exercise

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Abstract

This study examined the effects of human pregnancy and advancing gestation on the intensity of respiratory discomfort (dyspnea) during cycle exercise. Fourteen pregnant women (PG) performed a progressive cycle ergometer exercise test involving 20 W/min increases in work rate to symptom limitation and/or a heart rate of 170–175 beats/min at 19.7 ± 1.2 weeks (ENTRY), 28.2 ± 0.3 weeks (TM_2) and 36.3 ± 0.3 weeks (TM_3) gestation. Eight, age-matched, sedentary non-pregnant women (CG) were also studied for comparison purposes. Measurements included dyspnea intensity (Borg scale), minute ventilation ($\dot{V}_E$), breathing pattern and other cardiorespiratory parameters. At peak exercise, neither pregnancy nor advancing gestation had an effect on dyspnea, $\dot{V}_E$, breathing pattern, oxygen uptake or work rate ($p > 0.05$). $\dot{V}_E$ was significantly greater (by 11 L/min at 100 W) in the PG at TM_3 versus CG ($p < 0.05$) at all submaximal work rates. $\dot{V}_E$ also increased progressively from ENTRY to TM_2 and TM_3 during submaximal exercise. Dyspnea was not significantly different at any submaximal work rate in the PG at TM_3 versus CG or with advancing gestation in the PG. In addition, dyspnea at a standardized exercise $\dot{V}_E$ of 40 L/min was not different at TM_3 versus ENTRY or in the PG at TM_3 versus CG. Neither pregnancy nor advancing gestation were associated with increased respiratory discomfort during strenuous non-weight bearing cycle ergometer exercise, despite substantial increases in $\dot{V}_E$ and progressive mechanical adaptations of the respiratory system to accommodate the increasing size of the gravid uterus.

Keywords: Pregnancy; Advancing gestation; Respiratory discomfort; Exercise; Ventilation; Respiratory mechanics

1. Introduction

Human pregnancy is characterized by significant increases in ventilatory drive and minute ventilation ($\dot{V}_E$) at rest and during exercise (Contreras et al., 1991; Field et al., 1991; Wolfe et al., 1994; Lotgering et al., 1998; Ohtake and Wolfe, 1998; Heenan and Wolfe, 2000; Jensen et al., 2005). These changes are (1) accomplished by increases in tidal volume (V_T) with little or no change in respiratory frequency (f_R) (Contreras et al., 1991; Field et al., 1991; Ohtake and Wolfe, 1998), (2) established early in the first trimester (<8 weeks) (Wolfe et al., 1998; Weissgerber et al., 2006) and (3) determined, at least in part, by the stimulatory effects of gestational hormones on central and peripheral chemoreflex, and non-chemoreflex drives to breathe (Moore et al., 1987; Wolfe et al., 1998; Jensen et al., 2005).

It is reasonable to assume that pregnancy-induced increases in exercise $\dot{V}_E$, in addition to mechanical alterations in the shape and configuration of the abdomen, diaphragm and chest wall (secondary to increased size of the gravid uterus), may increase the perception of respiratory discomfort (dyspnea) during exercise in pregnancy, particularly in late gestation. Indeed, Milne et al. (1978) found that approximately 75% of healthy pregnant women with no history of cardiorespiratory disease complained of dyspnea upon exertion (i.e., stair climbing) by 31 weeks gestation. Despite the high prevalence of dyspnea in pregnancy, studies into its etiology are limited and the results are conflicting.

The earliest studies of gestational dyspnea hypothesized that it may be due to normal awareness of maternal hyperventila-

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tion (Cugell et al., 1953), increased respiratory effort (or work) secondary to mechanical alterations of the respiratory system (Bader et al., 1959) or an exaggerated awareness of normal $\dot{V}_E$ or respiratory effort (Gilbert et al., 1962; Gilbert and Auchincloss, 1966).

More recently, Field et al. (1991) showed that $\dot{V}_E$, V_T, inspiratory esophageal pressure swings (an index of inspiratory effort) and Borg dyspnea ratings were significantly greater during submaximal cycling exercise in late gestation versus the post-partum (PP) state suggesting that increases in respiratory discomfort may be due to the increased inspiratory effort that accompanies increased $\dot{V}_E$ during maternal exercise and not restricted ventilatory mechanics. However, in that study comparisons were made at a standardized work rate of only 48 W, corresponding to Borg dyspnea ratings of only 1.8 ± 1.4 ("very slight" to "slight") and 1.0 ± 0.9 ("very slight") in the pregnant and PP conditions, respectively. The ventilatory response at this low work rate may not be sufficient to unmask a potential mechanical ventilatory constraint to exercise in this population.

A previous study from this laboratory (Ohtake and Wolfe, 1998) which was designed to evaluate the impact of physical conditioning on aerobic working capacity in pregnancy, reported no effect of pregnancy or advancing gestation on ratings of perceived respiratory effort (RPEr) using Borg's 6–20 scale during light (20 W), moderate (45 W) and heavy (65 W) steady-state cycle ergometer exercise, despite significant increases in $\dot{V}_E$ and V_T at each work rate. Again, comparisons were made at modest submaximal steady-state work rates corresponding to RPEr ratings between 8 ("extremely light" to "very light") and 12 ("light" to "somewhat hard"). Furthermore, in that study RPEr (and not specifically dyspnea) was quantified only as a secondary outcome variable.

Unfortunately, no definitive conclusion regarding the physiological underpinnings of respiratory discomfort during exercise in pregnancy can be made from the existing literature because of considerable between-study differences in the specific instruction given to participants as to what qualitative dimension of respiratory discomfort they were being asked to scale (i.e., respiratory effort versus dyspnea), the mode of exercise employed (i.e., weight bearing versus non-weightbearing) and the testing protocol (i.e., incremental versus submaximal constant-load).

Therefore, the purpose of this study was to examine the effects of human pregnancy and advancing gestation on ratings of perceived respiratory discomfort during strenuous non-weight bearing cycle ergometer exercise. We hypothesized that ratings of exertional respiratory discomfort would increase with advancing gestation and would also be greater in pregnant versus non-pregnant women at a standardized work rate and $\dot{V}_E$ during exercise. To test this hypothesis, we conducted progressive cardiopulmonary cycle ergometer exercise testing (CPET) in 14 healthy, pregnant women at approximately 20, 28 and 36 weeks gestation and 8 age-matched non-pregnant control subjects. We measured and compared $\dot{V}_E$, breathing pattern, metabolic parameters and exertional symptoms at rest, throughout exercise and at a standardized $\dot{V}_E$.

2. Methods

2.1. Subjects

Subjects included 14 healthy, women (PG), 20–40 years, parity ≤ 3, who were experiencing healthy singleton pregnancies. A control group (CG) of eight healthy, age-matched (20–40 years), nulliparous, eumennorheic women was also studied to demonstrate the effects of human pregnancy on cardiorespiratory and perceptual responses to progressive exercise. Specific exclusion criteria for both groups included: history of cardiorespiratory disease; regular participation in strenuous occupational or recreational physical activity (>2 days/week); smoking history; taking medications (other than prenatal vitamins) that could contribute to dyspnea and exercise intolerance.

Subjects were recruited via posted announcements, newspaper advertisements and contact with local obstetricians and health care providers. Prior to study participation, pregnant subjects completed the Physical Activity Readiness Medical Examination for Pregnancy (http://www.csep.ca/forms.asp) and obtained medical clearance from the health care provider monitoring their pregnancies. Non-pregnant subjects completed the Physical Activity Readiness Questionnaire (http://www.csep.ca/forms.asp) to ensure there were no contraindications to CPET. Prior to experimental testing, qualified subjects attended an information session to become familiar with the laboratory and study procedures. The study protocol and consent form were approved by the Research Ethics Board, Faculty of Health Sciences, Queen's University and informed consent was obtained from all subjects.

2.2. Experimental design

As an incentive for study participation, pregnant subjects participated in a closely monitored prenatal muscle conditioning program designed to: promote proper posture; prevent low back pain, diastasis recti and urinary incontinence; strengthen the pelvic floor; and maintain general muscular fitness without causing improvement in the aerobic energy system. During these sessions maternal cardiac frequency (f_H) was maintained at <110 beats/min (as verified by regular pulse rate checks). Pregnant subjects participated in 1.7 ± 0.3 and 1.5 ± 0.4 (mean $\pm$ S.E.M.) muscular conditioning sessions/week in TM_2 and TM_3, respectively. Non-pregnant volunteers continued their sedentary lifestyles, avoiding regular participation in aerobic-type activity.

Pregnant subjects participated in CPET between 15 and 20 weeks gestation (ENTRY), at the end of TM_2 (25–27 weeks) and TM_3 (34–36 weeks). Non-pregnant subjects were tested during the follicular phase of their menstrual cycle and three were using oral contraceptives. Menstrual cycle phase was calculated using the first day of the last menstrual cycle and the average length of the cycle. We have previously validated this approach by simultaneous plasma progesterone measurements (Preston et al., 2001). Basic physical measurements included height, body mass and forced vital capacity (FVC) (S-301 Pneumoscan spirometry; KL Engineering Co., Slymar, CA). Predicted normal values for

FVC were those of Morris et al. (1971). Body mass index (BMI) was calculated as body mass/height^2. Subjects also performed CPET (described below).

2.3. Symptom evaluation

Respiratory discomfort (dyspnea) was defined as "the sensation of labored or difficult breathing" and leg discomfort as "the level of difficulty experienced during pedaling". Before exercise testing, subjects were familiarized with Borg's 0–10 category ratio scale (Borg, 1982) and its endpoints were anchored such that "0" represented "no respiratory discomfort (leg discomfort)" and "10" was "the most severe respiratory discomfort (leg discomfort) they had ever experienced or could ever imagine experiencing". By pointing to the Borg scale, subjects rated their level of perceived respiratory and leg discomfort at rest, every minute throughout exercise and at exercise cessation.

2.4. Cardiopulmonary exercise testing

Subjects consumed a standard meal (350 kcal; 20% fat, 20% protein, 60% carbohydrate) approximately 2 h before exercise tests to minimize within- and between-subject differences in nutritional status. Repeated tests were conducted at approximately the same time of day for each subject to minimize circadian effects. In addition, subjects avoided strenuous exercise and caffeine on the day of testing.

Evidence-based guidelines for exercise during pregnancy (Davies et al., 2003) recommend that women participate in non-weight bearing exercise (e.g. stationary cycling) and avoid activities (e.g. treadmill) that increase the risk of loss of balance and fetal trauma. In addition, non-weight bearing exercises, such as stationary cycling, eliminate the confounding effects of maternal weight gain on measures of aerobic working capacity. Therefore, incremental exercise tests were conducted on an electronically braked cycle ergometer (Ergometrics 800 s; SensorMedics, Yorba Linda, CA). The protocol involved 5-min of quiet breathing through a mouthpiece with noseclips while subjects were seated comfortably on the cycle ergometer (i.e., rest). Subjects then cycled for 4-min at a constant work rate of 20 W followed by 20 W/min increases in work rate to symptom limitation and/or a f_H of 170–175 beats/min. f_H was recorded both electrocardiographically (Max-1; Marquette Electronics, Milwaukee, WI) and with a Polar Electro Vantage f_H monitor (Polar, Finland). Cardiorespiratory responses were measured on a breath-by-breath basis at rest and during exercise as previously described (Heenan and Wolfe, 2000) and included: $\dot{V}_E$, V_T, f_R, oxygen consumption ($\dot{V}_{O_2}$), carbon dioxide production ($\dot{V}_{O_2}$), respiratory exchange ratio (R), f_H, ventilatory equivalents for oxygen ($\dot{V}_E/\dot{V}_{O_2}$) and carbon dioxide ($\dot{V}_E/\dot{V}_{CO_2}$). Resting data were taken as the average of the last 3-min of quiet breathing. Similarly, the last 30-s of breath-by-breath data from each stage of exercise as well as the last 30-s of loaded cycling (i.e., peak) were averaged and used for analysis.

An incremental (versus steady-state) symptom-limited cycle ergometer exercise protocol was chosen for this study to (1) examine the effects of pregnancy and advancing gestation on peak aerobic working capacity, (2) examine the relationship between exertional respiratory discomfort and exercise tolerance in human pregnancy, (3) unmask a potential mechanical ventilatory constraint to exercise tolerance in human pregnancy and (4) permit comparison of submaximal exercise responses between the present study with those of Field et al. (1991) who employed a submaximal incremental cycle exercise protocol to examine the relationship between dyspnea and ventilation during exercise in pregnancy.

2.5. Statistical analyses

A one-way ANOVA for repeated measures (SigmaStat 3.10, Systat Software Inc., Point Richmond, CA) was used to identify the effects of advancing gestation (ENTRY versus TM_2 versus TM_3) on physical characteristics, as well as cardiorespiratory and perceptual responses at rest, each submaximal work rate, peak exercise and a standardized exercise $\dot{V}_E$. When significant F-ratios were observed, pairwise comparisons were made using Tukey's (HSD) test. Unpaired t-tests were used to detect differences between the PG at TM_3 and CG for measured variables at rest, each submaximal work rate, peak exercise and a standardized exercise $\dot{V}_E$.

Cardiorespiratory and perceptual responses were compared at a standardized exercise $\dot{V}_E$ of 40 L/min (iso-$\dot{V}_{E_{40}}$), representing the highest equivalent $\dot{V}_E$ achieved during exercise by all subjects. Cardiorespiratory and perceptual parameters at iso-$\dot{V}_{E_{40}}$ were calculated by linear interpolation between adjacent measurement points for each subject. All data are expressed as mean ± S.E.M. Results for all statistical tests were considered significant at $p < 0.05$.

3. Results

3.1. General

Nineteen pregnant women volunteered for this study; however, three dropped out due to poor compliance and two developed gestational hypertension and were excluded from participation prior to testing at TM_3. Thus complete data were available from 14 pregnant women.

Physical characteristics of the PG and CG are described in Table 1. Parity for the PG was: 0, $n = 7$; 1, $n = 5$; 2, $n = 1$; 3, $n = 1$. PG at ENTRY and CG were matched for age, body height and FVC. As expected, body mass and BMI increased with advancing gestation and were significantly greater at TM_3 versus CG. FVC did not differ between ENTRY, TM_2 and TM_3.

3.2. Effects of human pregnancy on cardiorespiratory and perceptual responses at rest and during exercise

At rest, $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$ and f_H were significantly greater at TM_3 versus CG (Table 2). Resting $\dot{V}_E$ was 3.5 L/min (40%) higher in the PG at TM_3 versus CG ($p < 0.05$) and was accomplished by modest increases in f_R ($p = 0.07$) with no change in V_T.

$\dot{V}_E/\dot{V}_{O_2}$ and $\dot{V}_E/\dot{V}_{CO_2}$ were significantly greater throughout exercise in the PG at TM_3 versus CG (Fig. 1). $\dot{V}_{CO_2}$, $\dot{V}_E$ and

Table 1
Effects of human pregnancy and advancing gestation on physical characteristics

Variable	Pregnant group ($n=14$)			Control group ($n=8$)
	ENTRY	TM_2	TM_3	
Gestational age (weeks)	19.7 ± 1.2	28.2 ± 0.3	36.2 ± 0.3	N/A
Age (years)	30.9 ± 0.9	–	–	26.9 ± 2.0
Height (cm)	162.3 ± 1.5	–	–	162.6 ± 2.5
Body mass (kg)	71.5 ± 2.5	77.6 ± 2.6*	81.2 ± 2.6*,†	62.3 ± 2.7‡
Body mass index (kg/m^2)	26.7 ± 0.9	29.0 ± 0.9*	30.3 ± 0.9*,†	23.2 ± 1.0‡
Forced vital capacity (L) (% predicted)	3.97 ± 0.15 (106 ± 3)	4.04 ± 0.17 (108 ± 4)	4.08 ± 0.16 (109 ± 4)	3.81 ± 0.18 (99 ± 4)

$^{*}p<0.05$ vs. ENTRY; $^{\dagger}p<0.05$ vs. TM_2. ‡Significant difference between PG at TM_3 vs. CG ($p<0.05$). TM_2: second trimester; TM_3: third trimester; N/A: not applicable.

Table 2
Effects of human pregnancy and advancing gestation on cardiorespiratory responses at rest

Variable	Pregnant group ($n=14$)			Control group ($n=8$)
	ENTRY	TM_2	TM_3	
$\dot{V}_{O_2}$ (mL/min)	340 ± 10	375 ± 16*	398 ± 13*	312 ± 12‡
$\dot{V}_{CO_2}$ (mL/min)	306 ± 13	327 ± 13	362 ± 14*,†	281 ± 10‡
R	0.90 ± 0.02	0.88 ± 0.01	0.91 ± 0.01	0.91 ± 0.02
$\dot{V}_E$ (L/min)	10.2 ± 0.6	10.7 ± 0.4	12.0 ± 0.5*,†	8.5 ± 0.4‡
V_T (mL)	741 ± 80	731 ± 39	714 ± 40	656 ± 66
f_R (breaths/min)	16.2 ± 1.3	16.3 ± 1.0	18.2 ± 1.3*,†	14.3 ± 1.4
f_H (beats/min)	90 ± 3	93 ± 3	94 ± 3	84 ± 4‡
$\dot{V}_E/\dot{V}_{O_2}$	30.0 ± 1.2	28.9 ± 0.7	30.2 ± 0.8	27.6 ± 1.6
$\dot{V}_E/\dot{V}_{CO_2}$	33.3 ± 1.0	32.9 ± 0.8	33.2 ± 0.9	30.2 ± 1.2

$^{*}p<0.05$ vs. ENTRY; $^{\dagger}p<0.05$ vs. TM_2. ‡Significant difference between PG at TM_3 vs. CG ($p<0.05$). TM_2: second trimester; TM_3: third trimester; $\dot{V}_{O_2}$: oxygen consumption; $\dot{V}_{CO_2}$: carbon dioxide production; R: respiratory exchange ratio; $\dot{V}_E$: minute ventilation; V_T: tidal volume; f_R: respiratory frequency; f_H: cardiac frequency; $\dot{V}_E/\dot{V}_{O_2}$: ventilatory equivalent for oxygen; $\dot{V}_E/\dot{V}_{CO_2}$: ventilatory equivalent for carbon dioxide.

f_R were significantly greater at TM_3 versus CG at submaximal work rates (Table 3), but were not different at peak exercise (Table 4). V_T was not different at any work rate in the PG at TM_3 versus CG (Tables 3 and 4). f_H at all submaximal work rates was not different at TM_3 versus CG (Table 3); however, peak f_H was significantly lower at TM_3 versus CG (Table 4).

Borg dyspnea ratings were not different in the PG at TM_3 versus CG at any given submaximal work rate and at peak exercise (Fig. 2), despite substantial increases in exercise $\dot{V}_E$ (in the order of 11 L/min at 100 W; Fig. 1) with pregnancy. Similarly, ratings of perceived leg discomfort were not different during exercise in pregnant versus non-pregnant women (Fig. 2).

Dyspnea at iso-$\dot{V}_{E_{40}}$ was not significantly different in the PG at TM_3 versus CG (Table 5). $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$ and f_H were significantly lower and $\dot{V}_E/\dot{V}_{O_2}$ and $\dot{V}_E/\dot{V}_{CO_2}$ were significantly higher at iso-$\dot{V}_{E_{40}}$ in the PG at TM_3 versus CG. f_R was higher ($p=0.07$) and V_T lower ($p=0.07$) at iso-$\dot{V}_{E_{40}}$ in the PG at TM_3; however, these trends did not reach significance. Finally, ratings of perceived leg discomfort and R were not different between TM_3 and CG at iso-$\dot{V}_{E_{40}}$.

Table 3
Effects of human pregnancy and advancing gestation on cardiorespiratory and perceptual responses during exercise at the highest equivalent work rate (100 W)

Variable	Pregnant group ($n=14$)			Control group ($n=8$)
	ENTRY	TM_2	TM_3	
Dyspnea (Borg)	3.0 ± 0.4	3.1 ± 0.5	3.0 ± 0.5	2.8 ± 0.5
Leg discomfort (Borg)	3.5 ± 0.3	3.4 ± 0.5	3.5 ± 0.6	3.3 ± 0.5
$\dot{V}_{O_2}$ (mL/min)	1180 ± 28	1238 ± 30	1283 ± 28*	1225 ± 22
$\dot{V}_{CO_2}$ (mL/min)	1251 ± 39	1278 ± 36	1341 ± 32*	1230 ± 38‡
R	1.06 ± 0.02	1.03 ± 0.02	1.05 ± 0.02	1.01 ± 0.04
$\dot{V}_E$ (L/min)	36.0 ± 1.8	37.8 ± 1.3	40.5 ± 1.4*	29.3 ± 1.4‡
V_T (mL)	1441 ± 61	1441 ± 56	1474 ± 68	1380 ± 70
f_R (breaths/min)	25.8 ± 1.7	27.5 ± 1.7	29.0 ± 1.8*	22.1 ± 1.2‡
f_H (beats/min)	136 ± 4	137 ± 4	138 ± 4	133 ± 7
$\dot{V}_E/\dot{V}_{O_2}$	30.5 ± 1.2	30.7 ± 0.9	31.7 ± 1.2	24.0 ± 1.5‡
$\dot{V}_E/\dot{V}_{CO_2}$	28.7 ± 0.9	29.7 ± 0.7	30.2 ± 0.9*	23.7 ± 0.6‡

$^{*}p<0.05$ vs. ENTRY; ‡significant difference between PG at TM_3 vs. CG ($p<0.05$). Refer to Table 2 footnote for definition of abbreviations.

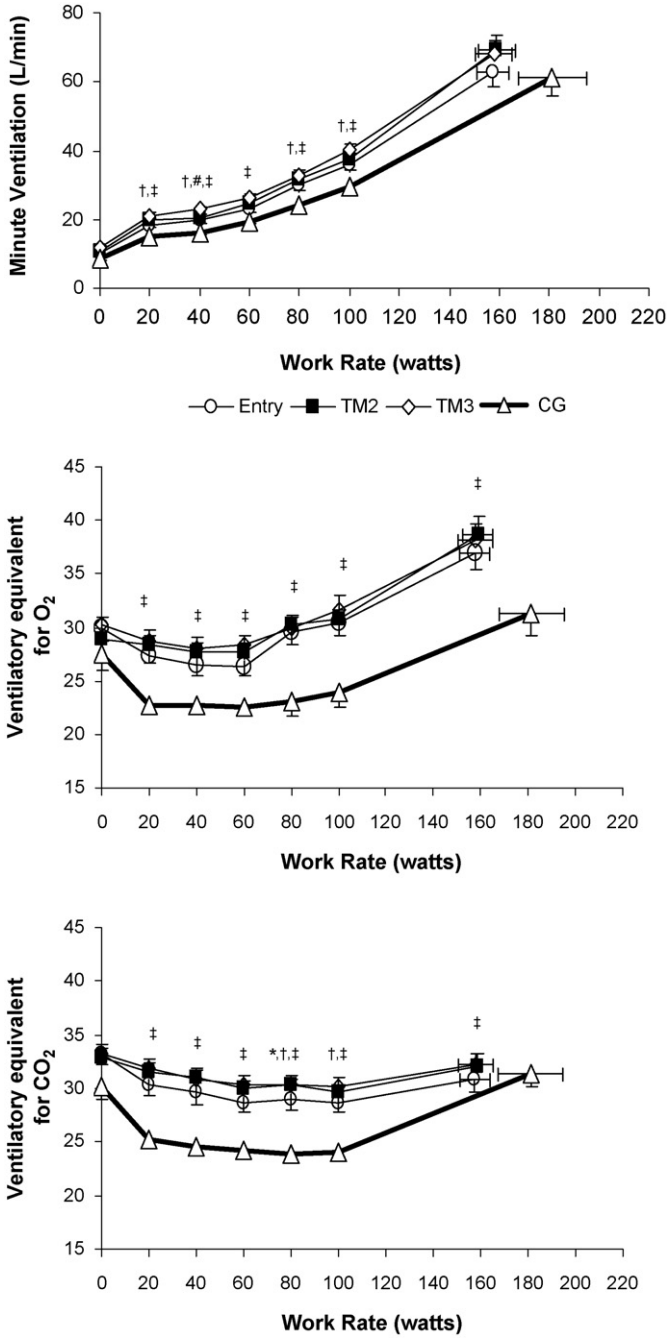

Fig. 1. Effects of human pregnancy and advancing gestation on the ventilatory response to progressive cycle ergometer exercise. TM_2, trimester two; TM_3, trimester three; O_2, oxygen; CO_2, carbon dioxide. *Significant difference between ENTRY and TM_2 ($p < 0.05$); †significant difference between ENTRY and TM_3 ($p < 0.05$); #significant difference between TM_2 and TM_3 ($p < 0.05$). ‡significant difference between PG at TM_3 and CG ($p < 0.05$).

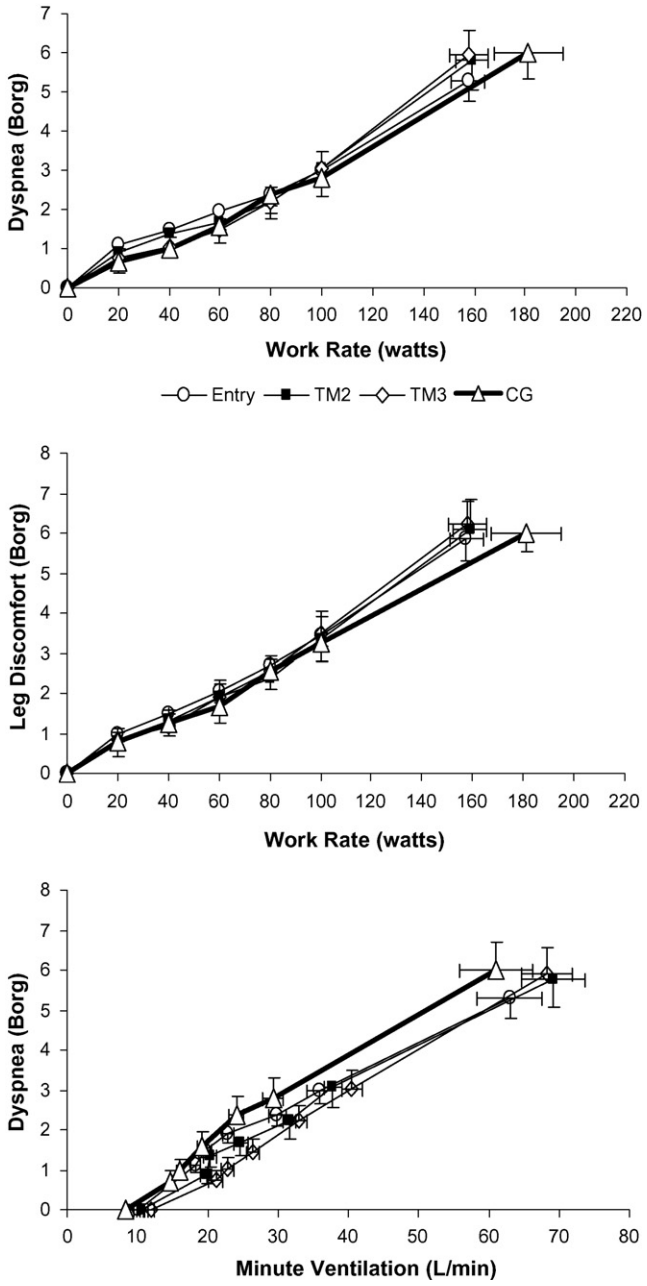

Fig. 2. Effects of human pregnancy and advancing gestation on the perceptual response to progressive cycle ergometer exercise. TM_2: trimester two; TM_3: trimester three.

3.3. Effects of advancing gestation on cardiorespiratory and perceptual responses at rest and during exercise

At rest, $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$, $\dot{V}_E$ and f_R increased from ENTRY to TM_2 and TM_3, respectively (Table 2). Advancing gestation had no effect on R, V_T, f_H, $\dot{V}_E/\dot{V}_{O_2}$ or $\dot{V}_E/\dot{V}_{CO_2}$ at rest.

Ventilatory responses to exercise are shown in Fig. 1. $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$ and $\dot{V}_E$ were significantly greater during submaximal exercise work rates at TM_3 versus ENTRY (Table 3). From TM_2 to TM_3, $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$ and $\dot{V}_E$ increased significantly during exercise at 40 W only. Advancing gestation had no effect on peak $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$ or $\dot{V}_E$ (Table 4). Advancing gestation had no significant effect on V_T during maternal exercise (Tables 3 and 4). f_R was significantly greater at TM_3 versus ENTRY during exercise at 100 W (Table 3). R, f_H and $\dot{V}_E/\dot{V}_{O_2}$ were not different between ENTRY, TM_2 or TM_3 at any work rate (Tables 3 and 4). $\dot{V}_E/\dot{V}_{CO_2}$ increased from ENTRY to TM_3 at 100 W (Table 3).

Borg ratings of respiratory discomfort during submaximal and peak exercise were not significantly different between ENTRY, TM_2 and TM_3 (Fig. 2), respectively, despite significant

Table 4
Effects of human pregnancy and advancing gestation on cardiorespiratory and perceptual responses at peak exercise

Variable	Pregnant group ($n=14$)			Control group ($n=8$)
	ENTRY	TM_2	TM_3	
Work rate (W)	158 ± 7 (range: 120–200)	159 ± 6 (range: 120–200)	158 ± 7 (range: 115–210)	181 ± 14 (range: 140–240)
Dyspnea (Borg)	5.3 ± 0.5	5.8 ± 0.7	5.9 ± 0.7	6.0 ± 0.7
Leg discomfort (Borg)	5.9 ± 0.5	6.1 ± 0.8	6.2 ± 0.6	6.0 ± 0.5
$\dot{V}_{O_2}$ (mL/min)	1701 ± 94	1794 ± 90	1798 ± 82	1975 ± 17
$\dot{V}_{CO_2}$ (mL/min)	2039 ± 114	2157 ± 109	2121 ± 85	2330 ± 166
R	1.20 ± 0.02	1.20 ± 0.02	1.19 ± 0.02	1.19 ± 0.04
$\dot{V}_E$ (L/min)	63.0 ± 4.6	69.2 ± 4.5	68.2 ± 3.6	61.0 ± 5.2
V_T (mL)	1893 ± 104	1917 ± 82	1886 ± 84	1895 ± 16
f_R (breaths/min)	33.8 ± 1.7	36.9 ± 2.1	36.9 ± 3.0	32.5 ± 1.5
f_H (beats/min)	166 ± 1	165 ± 2	164 ± 2	173 ± 1‡
$\dot{V}_E/\dot{V}_{O_2}$	37.0 ± 1.7	38.7 ± 1.7	38.2 ± 1.5	31.3 ± 2.2‡
$\dot{V}_E/\dot{V}_{CO_2}$	30.8 ± 1.2	32.1 ± 1.2	32.2 ± 1.1	26.1 ± 1.2‡

*$p<0.05$ vs. ENTRY; ‡significant difference between PG at TM_3 vs. CG ($p<0.05$). Refer to Table 2 footnote for definition of abbreviations.

Table 5
Effects of human pregnancy and advancing gestation on cardiorespiratory and perceptual responses at a standardized exercise ventilation of 40 L/min

Variable	Pregnant group ($n=14$)			Control group ($n=8$)
	ENTRY	TM_2	TM_3	
Dyspnea (Borg)	3.5 ± 0.3	3.2 ± 0.5	3.0 ± 0.4	3.9 ± 0.6
Leg discomfort (Borg)	4.0 ± 0.3	3.5 ± 0.5	3.5 ± 0.4	4.3 ± 0.5
$\dot{V}_{O_2}$ (mL/min)	1281 ± 40	1277 ± 32	1294 ± 45	1542 ± 80‡
$\dot{V}_{CO_2}$ (mL/min)	1398 ± 44	1349 ± 30	1345 ± 42	1678 ± 53‡
R	1.09 ± 0.02	1.06 ± 0.02*	1.04 ± 0.02*	1.10 ± 0.03
V_T (mL)	1523 ± 83	1525 ± 80	1461 ± 96	1735 ± 107
f_R (breaths/min)	27.8 ± 1.6	27.7 ± 1.5	29.0 ± 1.7	24.2 ± 1.4
f_H (beats/min)	142 ± 4	140 ± 4	138 ± 3	151 ± 5‡
$\dot{V}_E/\dot{V}_{O_2}$	31.6 ± 1.0	31.6 ± 0.8	31.4 ± 1.0	26.5 ± 1.3‡
$\dot{V}_E/\dot{V}_{CO_2}$	28.9 ± 0.9	29.8 ± 0.7	30.0 ± 0.9	24.3 ± 0.7‡

*$p<0.05$ vs. ENTRY; ‡significant difference between PG at TM_3 vs. CG ($p<0.05$). Refer to Table 2 footnote for definition of abbreviations.

increases in exercise $\dot{V}_E$ with advancing gestation (Fig. 1). Also, ratings of perceived leg discomfort were not different during submaximal and peak exercise at ENTRY, TM_2 and TM_3 (Fig. 2).

Advancing gestation had no effect on dyspnea at iso-$\dot{V}_{E_{40}}$ (Table 5). Cardiorespiratory parameters and ratings of perceived leg discomfort at iso-$\dot{V}_{E_{40}}$ did not change with advancing gestation. However, R at iso-$\dot{V}_{E_{40}}$ decreased from ENTRY to TM_2 and TM_3, respectively.

4. Discussion

The main findings of this study are that neither pregnancy nor advancing gestation were associated with increased respiratory discomfort during strenuous non-weight bearing cycle ergometer exercise despite significant increases in exercise $\dot{V}_E$ and progressive thoraco-abdominal distortion. Second, Borg ratings of respiratory discomfort at iso-$\dot{V}_{E_{40}}$ were not increased as a result of pregnancy or advancing gestation, suggesting mechanical adaptation of the respiratory system.

In pulmonary disease states, dyspnea intensity is positively correlated with the level of $\dot{V}_E$ (absolute or relative to maximal ventilatory capacity) and inspiratory effort (absolute or relative to maximal inspiratory pressure) during exercise (LeBlanc et al., 1986; Marciniuk et al., 1994). Human pregnancy is characterized by substantial increases in exercise $\dot{V}_E$ (Contreras et al., 1991; Field et al., 1991; Wolfe et al., 1994; Lotgering et al., 1998; Ohtake and Wolfe, 1998; Heenan and Wolfe, 2000) and inspiratory effort (Field et al., 1991), with no demonstrable effect on maximal voluntary ventilation (Berry et al., 1989) or diaphragmatic muscle strength (Gilroy et al., 1988; Contreras et al., 1991; Field et al., 1991). Therefore, increased levels of $\dot{V}_E$ during exercise in pregnancy and advancing gestation may increase ratings of exertional respiratory discomfort.

In addition, it is reasonable to suggest that progressive thoraco-abdominal distortion, secondary to the expanding uterus (Weinberger et al., 1980; Elkus and Popovich, 1992; Crapo, 1996), may compromise the mechanical response of the respiratory system during exercise, particularly in late gestation. Consequently, more effort (or work) may be required to achieve a given level of $\dot{V}_E$ during exercise, which would provoke an increase in respiratory discomfort. Field et al. (1991) demonstrated that $\dot{V}_E$, V_T, inspiratory effort and Borg dyspnea ratings were significantly greater at 48 W of cycle exercise in late gestation versus the post-partum (PP) state. In addition,

relationships between inspiratory effort and V_T and between dyspnea and inspiratory effort were not different in the pregnant and PP conditions, suggesting that pregnancy-induced increases in exertional dyspnea reflect the normal awareness of increased inspiratory effort that accompanies increased $\dot{V}_E$ during maternal exercise and not restricted ventilatory mechanics. In that study, however, third trimester exercise tests were stopped when the subjects achieved 70% of their predicted maximum f_H and, therefore, comparisons were made at a standardized work rate of only 48 W. At this low work rate, Borg dyspnea ratings were only 1.8 ± 1.4 ("very slight" to "slight") and 1.0 ± 0.9 ("very slight") in the third trimester and PP conditions, respectively. Given the low dyspnea intensity ratings it is unclear whether these patients actually experienced significant respiratory discomfort. In addition, the submaximal exercise testing protocol employed by Field et al. (1991) may have been too conservative to challenge the limits of the respiratory system and unmask a potential mechanical ventilatory constraint to exercise in pregnancy. Therefore, it is difficult to make direct comparisons between the present study results with those of Field et al. (1991).

To our surprise and in contrast to the above, Borg dyspnea ratings did not increase during cycle exercise in the PG at TM_3 versus CG or from ENTRY to TM_2 and TM_3, respectively, despite significant increases in exercise $\dot{V}_E$. To this end, $\dot{V}_E$ was approximately 11 L/min (40%) higher during exercise at the highest equivalent work rate (100 W) in the PG at TM_3 versus CG; however, dyspnea intensity was not increased in the former. These results are consistent with a previous report by Ohtake and Wolfe (1998) who examined cardiorespiratory and RPEr responses to light (20 W), moderate (45 W) and heavy (65 W) steady-state cycle exercise in 20 healthy women at approximately 18, 27 and 37 weeks gestation and 3 months PP. In accordance with the present study, significant increases in $\dot{V}_E$, $\dot{V}_E/\dot{V}_{CO_2}$ and $\dot{V}_E/\dot{V}_{O_2}$ were observed at all three work rates in the pregnant versus PP state (Ohtake and Wolfe, 1998). $\dot{V}_E$ and $\dot{V}_E/\dot{V}_{CO_2}$ were also significantly greater during exercise at 37 versus 18 weeks gestation, particularly at higher work rates, which is in good agreement with our results. Despite these differences, no measurable changes in RPEr were observed at any work rate during pregnancy or with advancing gestation (Ohtake and Wolfe, 1998). In that study, however, RPEr was not a primary outcome variable, comparisons were made at modest submaximal steady-state work rates corresponding to RPEr ratings between 8 and 12 ("extremely light" to "somewhat hard"), the qualitative dimension of RPEr was not defined for the subjects and the end-points of the Borg 6–20 scale were not anchored prior to exercise. Therefore, it may not be possible to directly compare the present study results with those of Ohtake and Wolfe (1998).

Unlike most previous studies (Contreras et al., 1991; Field et al., 1991; Ohtake and Wolfe, 1998), pregnancy-induced increases in $\dot{V}_E$ at rest and during exercise in this study could be explained by increased f_R with no change in V_T. The reason for this difference is not clear. It is possible that increasing $\dot{V}_E$ by increasing f_R has no effect on the sensation of exertional dyspnea as observed in this study whereas increasing $\dot{V}_E$ by increasing V_T may increase dyspnea as seen by others (Field et al., 1991). However, this is unlikely since Ohtake and Wolfe (1998) reported no change in RPEr during submaximal steady-state cycle exercise in pregnancy and advancing gestation, despite significant increases in $\dot{V}_E$ and V_T with no change in f_R.

Gilbert et al. (1962) and Gilbert and Auchincloss (1966) hypothesized that gestational dyspnea may be due to an exaggerated central perception of $\dot{V}_E$ or respiratory effort. If this hypothesis were true then dyspnea would be greater at any given $\dot{V}_E$ or respiratory effort during exercise in the pregnant versus non-pregnant state. In this study, however, dyspnea was approximately 1 Borg unit lower in the PG at TM_3 versus CG ($p = 0.17$) and not different at TM_3 versus ENTRY, despite significant thoraco-abdominal distortion secondary to a 10 kg (14%) increase in maternal body mass from ENTRY to TM_3 and a 19 kg difference in body mass between the PG at TM_3 and CG. Similarly, Ohtake and Wolfe (1998) reported a decrease in the RPEr-$\dot{V}_E$ relationship during light, moderate and heavy submaximal steady-state cycle exercise in late gestation versus PP. Finally, Field et al. (1991) demonstrated that the relationship between dyspnea intensity and inspiratory effort was preserved during submaximal exercise in late gestation. Taken together, the central perception of respiratory effort may be unchanged or even slightly reduced during exercise in pregnancy and throughout gestation.

Detailed measures of pulmonary function, resting and dynamic operating lung volumes, airway resistance/function and respiratory mechanics were not obtained in this study and, therefore, our ability to interpret and discuss the results is limited. Notwithstanding these limitations, the proceeding discussion addresses possible explanations for the lack of anticipated increase in respiratory discomfort during maternal exercise using results from published studies in human pregnancy, health and disease. Possible explanations may include (1) desensitization to exertional respiratory discomfort during pregnancy and (2) compensatory adaptations in baseline ventilatory mechanics.

We cannot rule out the possibility that during the course of human pregnancy, temporal desensitization to the sensory consequences of an increased ventilatory drive and relative hyperventilation somehow obviates the expected increase in perceived respiratory discomfort during cycle exercise. To our knowledge no studies have been undertaken to compare sensory detection thresholds for external mechanical loads in the pregnant versus non-pregnant state. However, one would not anticipate blunted sensory responsiveness during pregnancy given the increased amplitude of the chemical and non-chemical drives to breathe that characterize this condition (Moore et al., 1987; Wolfe et al., 1998; Jensen et al., 2005).

Plasma β-endorphin concentrations are significantly greater at rest and during exercise in pregnancy (McMurray et al., 1990). In addition, the β-endorphin response to exercise is reportedly magnified in pregnant women (McMurray et al., 1990). Thus, increased β-endorphin levels may desensitize the central perception of respiratory effort such that the intensity of respiratory discomfort during maternal exercise is unchanged, despite changes in $\dot{V}_E$ and ventilatory mechanics. Increased β-endorphin release would be expected to attenuate the $\dot{V}_E$ response to exer-

cise and would not, therefore, alter dyspnea-$\dot{V}_E$ relationships throughout exercise as occurred in our study participants. Moreover, if β-endorphins modulated central perception of global effort from respiratory and other peripheral skeletal muscles one would anticipate a decrease in the intensity of perceived leg discomfort at any given work rate in pregnant versus non-pregnant women. However, this was not the case as Borg ratings of leg discomfort were not different throughout exercise in the PG at TM_3 versus CG of the present study.

O'Donnell et al. (2000) previously demonstrated that increasing ventilatory drive by dead space loading during exercise in young healthy men had no effect on the slope or position of the dyspnea-$\dot{V}_E$ response curve, provided the mechanical response of the respiratory system was not constrained. However, in that study, imposing a mechanical constraint to V_T expansion by chest wall strapping caused a dramatic upwards shift of the dyspnea-$\dot{V}_E$ response curve, such that dyspnea intensity at any given $\dot{V}_E$ during exercise was significantly greater compared to the mechanically unloaded condition. Similarly, hyperoxia-induced reductions in ventilatory drive during exercise in patients with chronic obstructive pulmonary disease had no effect on the dyspnea-$\dot{V}_E$ relationship whereas mechanical unloading reduced dyspnea intensity at any given exercise $\dot{V}_E$ (Peters et al., 2006). These data suggest that a change in dyspnea intensity at a standardized $\dot{V}_E$ during exercise in both health and disease reflects a change in ventilatory mechanics, independent of ventilatory drive/demand. Since pregnancy-induced increases in exercise $\dot{V}_E$ and ventilatory drive are almost fully established by the eighth week of gestation (Weissgerber et al., 2006) progressive mechanical ventilatory constraints with advancing gestation (secondary to thoraco-abdominal distention with attendant reductions in chest wall and respiratory system compliance) would become the dominant contributor to dyspnea at any given $\dot{V}_E$ during exercise. However, Borg dyspnea ratings at iso-$\dot{V}_{E_{40}}$ were not different at TM_3 versus ENTRY. In addition, dyspnea was approximately 1 Borg unit lower in the PG at TM_3 versus CG ($p = 0.17$) even though $\dot{V}_E/\dot{V}_{CO_2}$ (i.e., ventilatory drive) and $\dot{V}_E/\dot{V}_{O_2}$ (i.e., ventilatory demand) were significantly greater. These data suggest that the mechanical response of the respiratory system may be preserved during exercise in healthy human pregnancy.

It is possible that mechanical adaptations of the respiratory system including altered resting and dynamic operating lung volumes and reduced airways resistance, preserve ventilatory mechanics and minimize the work of breathing and, therefore, respiratory discomfort in the setting of increased $\dot{V}_E$ during maternal exercise. Human pregnancy is characterized by significant and consistent changes in lung volumes and capacities that are identifiable by approximately 15 weeks gestation and progress to term (Knuttgen and Emerson, 1974; Gilroy et al., 1988; Berry et al., 1989; Contreras et al., 1991). These changes include a 15–20% (400–500 mL) reduction in end-expiratory lung volume (EELV) secondary to reductions in expiratory reserve volume, with little or no change in residual volume (Knuttgen and Emerson, 1974; Gilroy et al., 1988; Berry et al., 1989; Contreras et al., 1991). The reduction in EELV is effectively offset by a 15–20% (300–400 mL) increase in resting inspiratory capacity (IC) such that total lung capacity does not change (Knuttgen and Emerson, 1974; Contreras et al., 1991). Since residual volume and total lung capacity are preserved during pregnancy vital capacity does not change, as confirmed by our results. Therefore, V_T expansion during maternal exercise within an already increased IC may preserve the relationship between inspiratory effort and volume displacement thereby avoiding encroachment of end-inspiratory lung volume on the upper alinear extreme of the respiratory system's sigmoidal pressure–volume curve where (1) V_T expansion is constrained, (2) work of breathing is increased and (3) severe dyspnea is provoked (O'Donnell, 2006). Thus, recruitment of resting IC would, at least in theory, preserve neuromechanical coupling of the respiratory system in the transition from rest to peak exercise and may explain why dyspnea did not increase despite increased $\dot{V}_E$ and ventilatory drive during maternal exercise in this study.

The role of reduced airways resistance as a potentially important ventilatory adaptation to pregnancy remains to be determined. Pregnancy-induced reductions in EELV (Knuttgen and Emerson, 1974; Gilroy et al., 1988; Berry et al., 1989; Contreras et al., 1991) and arterial P_{CO_2} (Jensen et al., 2005) in addition to increased circulating estrogen concentrations (Jensen et al., 2005) would be expected to increase flow resistance of the upper and lower airways (Briscoe and DuBois, 1958; Newhouse et al., 1964; Elkus and Popovich, 1992; Crapo, 1996). Despite these changes, however, neither pregnancy nor advancing gestation have an effect on forced expiratory volumes (Milne et al., 1977; Knuttgen and Emerson, 1974; Berry et al., 1989) or peak expiratory flow rates (Brancazio et al., 1997), suggesting lower airway resistance and bronchodilation. In fact, airway resistance has been shown to decrease in human pregnancy (Rubin et al., 1956; Gee et al., 1967; Garrard et al., 1978). It is possible that pregnancy-induced increases in circulating progesterone (a potent smooth muscle relaxant) decrease airway resistance by a direct bronchodilatory action thereby minimizing the oxygen cost of breathing. This progesterone-dependent bronchodilation could explain why Borg dyspnea ratings at iso-$\dot{V}_{E_{40}}$ were slightly reduced in our study. A comparison of iso-volume tidal respired flow rates at a standardized exercise $\dot{V}_E$ during the pregnant and post-partum period would be required to conclusively evaluate the potential role of pregnancy-induced bronchodilation in minimizing the oxygen cost of breathing and perhaps, therefore, dyspnea.

4.1. Summary

Pregnant women experienced no increase in respiratory discomfort, despite substantial increases in $\dot{V}_E$ during progressive non-weight bearing cycle ergometer exercise in pregnancy and throughout gestation. In addition, Borg ratings of respiratory discomfort at a standardized exercise $\dot{V}_E$ of 40 L/min were not increased as a result of pregnancy or advancing gestation, suggesting mechanical adaptation of the respiratory system. Studies that include detailed examination of pulmonary function, respiratory mechanics, operating lung volumes, $\dot{V}_E$, breathing pattern and dyspnea intensity during exercise in the pregnant and postpartum period are required.

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