Pulmonary Mechanics and Gas Exchange during Exercise in Kenyan Distance Runners

GLEN E. FOSTER[1], MICHAEL S. KOEHLE[1,2], PAOLO B. DOMINELLI[1], FRANCIS M. MWANGI[3], VINCENT O. ONYWERA[3], MICHAEL K. BOIT[3], JOSHUA C. TREMBLAY[4], CHEPLETING BOIT[3], and A. WILLIAM SHEEL[1]

[1]School of Kinesiology, University of British Columbia, Vancouver, BC, CANADA; [2]Division of Sports Medicine, University of British Columbia, Vancouver, BC, CANADA; [3]Department of Recreation Management and Exercise Science, Kenyatta University, Nairobi, KENYA; and [4]Department of Human Health and Nutritional Sciences, University of Guelph, Guelph, ON, CANADA

BASIC SCIENCES

ABSTRACT

FOSTER, G. E., .M. S. KOEHLE, P. B. DOMINELLI, F. M. MWANGI, V. O. ONYWERA, M. K. BOIT, J. C. TREMBLAY, C. BOIT, and A. W. SHEEL. Pulmonary Mechanics and Gas Exchange during Exercise in Kenyan Distance Runners. *Med. Sci. Sports Exerc.*, Vol. 46, No. 4, pp. 702–710, 2014. **Purpose**: The purpose of this study was to determine arterial blood gases, the mechanical limits for generating expiratory flow and the work performed by the respiratory muscles during treadmill exercise in Kenyan runners. **Methods**: Kenyan runners (10 men and 4 women; mean ± SD age = 25.2 ± 1.3 yr) were instrumented with a radial artery catheter, an esophageal balloon-tipped catheter, and an esophageal temperature probe for the determination of blood gases, the work of breathing and core temperature, respectively. Testing occurred at 1545 m above sea level. **Results**: There were significant decreases in the arterial partial pressure of O_2 and oxyhemoglobin saturation and a widening of the alveolar-to-arterial difference in O_2 from rest to peak exercise. The mechanical work of breathing increased with increasing minute ventilation and was commensurate with values expected for treadmill running in elite athletes. During heavy exercise, significant expiratory flow limitation was present in half of the subjects while the remaining subjects demonstrated impending flow limitation. **Conclusions**: Pulmonary system limitations were present in Kenyan runners in the form of exercise-induced arterial hypoxemia, expiratory flow limitation, and high levels of respiratory muscle work. It appears that Kenyan runners do not posses a pulmonary system that confers a physiological advantage.
Key Words: EXERCISE HYPERPNEA, EXPIRATORY FLOW LIMITATION, WORK OF BREATHING, HYPOXEMIA

Runners from Kenya have dominated international running events ranging from the 800 m to the marathon over the last four decades (22,25). Most elite Kenyan runners come from the Rift Valley province and self-identify as belonging to the Kalenjin ethnic group (25). Why are Kenyan runners from a small geographical region and common ancestry disproportionately successful and what might be the physiological basis of their superior athletic performances? The answer to this question is unclear, but running economy, the fractional use of maximal oxygen uptake ($\dot{V}O_{2max}$), and oxidative enzyme activity appear higher in Kenyan runners relative to non-Kenyan runners (5,32,33). However, when comparing Kenyan to elite non-Kenyan runners, there are no differences in several variables associated with exercise performance, including $\dot{V}O_{2max}$, total hemoglobin mass, blood volume, muscle fiber size and composition, muscle capillarization, and citrate synthase activity (28,32,33).

There is now sufficient evidence demonstrating that in some highly trained male endurance athletes, the lung's diffusion surface, airways, and chest-wall musculature are relatively "underbuilt" relative to the demand for maximal O_2 transport during exercise. Reported pulmonary system limitations to exercising humans include (i) exercise-induced arterial hypoxemia (EIAH) (9); (ii) expiratory flow limitation (EFL) (20), and (iii) high levels of respiratory muscle work leading to fatigue of the diaphragm and a redistribution of cardiac output (19,35). The above-mentioned pulmonary system limitations are important determinants of exercise performance, but to our knowledge, there are no published reports dealing with the pulmonary responses to exercise in Kenyan runners. In the present study, we questioned whether Kenyan runners experience pulmonary limitations during exercise as has been commonly reported in other endurance athletes. To this end, the purpose of this study was to determine

Address for correspondence: A. William Sheel, Ph.D., School of Kinesiology, University of British Columbia, 6108 Thunderbird Blvd, Vancouver, BC, V6T-1Z3, Canada; E-mail: bill.sheel@ubc.ca.
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arterial blood gases, the mechanical limits for generating expiratory flow, and the work performed by the respiratory muscles during treadmill exercise in Kenyan runners.

METHODS

Subjects. Fourteen elite Kenyan runners (10 men and 4 women) specializing in running distances ranging from 800 m to the marathon were recruited to participate in this study. The Research Ethics Board of the University of British Columbia and Kenyatta University approved all experimental procedures. Participants competed in national and international running events with a range of racing accomplishments. Several subjects had principally competed at modest high altitude (1500–2150 m) in Kenya. One female participant was a former medalist at the Junior World Cross-Country Running Championships, while two male participants competed internationally at major marathons with personal best times of 2 h, 9 min. The exercise-training regime among athletes was variable depending on their respective competitive event. Training distances covered ranged from 50 to 180 $km \cdot wk^{-1}$, and the self-reported intensity was variable between subjects, but all reported regularly participating in high-intensity interval training. Most athletes performed two training sessions per day, 3–4 $d \cdot wk^{-1}$, and single sessions on other days. Participants' self-reported being physically active throughout childhood and adolescence by walking or running 2–10 km to school. All subjects were born at high altitude (2000–2400 m), and all but one male participant self-identified as being of Kalenjin ancestry. The remaining participant self-identified as being of Maasai ancestry.

Experimental protocol. Testing occurred at Kenyatta University, Nairobi, which is at 1545 m above sea level and can be classified as between low to moderate altitude (3). During the testing period, barometric pressure was consistent (635.0 ± 0.4 mm Hg) and corresponded to an FiO_2 of approximately 0.172 at sea level. Subjects with limited treadmill running experience were provided practice sessions before the experimental day. Upon reporting to the laboratory, subjects completed an informed consent form, medical, and running history questionnaires. Experimental procedures were explained in English and Kiswahili. Pulmonary function and anthropometric measures were obtained, and subjects were then instrumented with a radial artery catheter and an esophageal balloon-tipped catheter and temperature probe. Measurements of expired gases, respiratory parameters, and arterial blood were obtained during incremental treadmill running.

Pulmonary function. Forced vital capacity (FVC), forced expiratory volume in 1 s ($FEV_{1.0}$), $FEV_{1.0}$/FVC, and maximal inspiratory pressure tests were conducted in a seated position and conformed to standardized procedures by the American Thoracic Society. Values were expressed as percent predicted values based on Kenyan (26) and North American (16) normative data.

Graded treadmill exercise testing. The exercise protocol consisted of a 10- to 20-min warm-up period at a self-selected speed on a motorized treadmill (model T170; Cosmed, Rome, Italy). During the exercise test, subjects wore a chest harness attached to a support structure around the treadmill. The initial treadmill speed ranged from 9 to 13 $km \cdot h^{-1}$, depending on the subject's sex and estimated highest attainable speed, and was thereafter increased by 1 $km \cdot h^{-1}$ every 2.5 min to the point of exhaustion. The inclination of the treadmill was maintained at 1.5%, and work was calculated. Throughout testing, subjects wore nose clips and breathed through a mouthpiece connected to a nonrebreathing valve (model 2700B; Hans-Rudolph, Kansas City, MO). Mixed expired gases were measured using calibrated CO_2 and O_2 analyzers (models 17630 and 17625; Vacumed, Ventura, CA). For the purposes of determining minute ventilation and metabolic calculations, inspiratory flow was measured using a calibrated pneumotachograph (model 3813; Hans Rudolph, Kansas City, MO). Heart rate was recorded with a portable monitor (S610i; Polar Electro, Kempele, Finland).

Arterial blood sampling. Subjects had a 20-gauge catheter placed into the radial artery using sterile technique under local anesthesia using methods described elsewhere (10). Arterial blood was analyzed for PaO_2, $PaCO_2$, pH, SaO_2, [Hb], and Hct (Radiometer ABL Flex80, Copenhagen, DK), and HCO_3^- was calculated (34). Arterial blood gases were corrected for *in vivo* temperature changes during exercise as measured from a rapid response thermistor placed intranasally into the lower one-third of the esophagus (Physitemp Instruments, Clifton, NJ). The alveolar gas equation was used to calculate ideal alveolar oxygen tension (PAO_2) and the alveolar–arterial oxygen tension difference ($A\text{-}aDO_2$). Water vapor pressure was calculated using the subjects' measured esophageal temperature. Resting blood samples were drawn after a 15- to 25-min period of quiescence in the seated position while subjects breathed through a mouthpiece and mixed expired gases were measured. Blood samples were then obtained during the final 30 s of each stage of treadmill running. The proportion of SaO_2 change due to shifting of the O_2–Hb dissociation curve (via temperature, pH and $PaCO_2$) and changes in PaO_2 were calculated independently. To determine the SaO_2 changes that were due to reductions PaO_2, an ideal resting O_2-Hb curve (temperature = 37°C; pH 7.40; $PaCO_2$ = 40 mm Hg) was applied to the measured PaO_2. To determine the extent to which exercise-induced shifts of the O_2–Hb dissociation curve affected SaO_2, resting PaO_2 was applied to a curve with temperature, pH, and $PaCO_2$ accounted for.

In addition to direct measurement by the blood gas analyzer, S_aO_2 was calculated as though pH, temperature, and PaO_2 remained unchanged from ideal resting conditions (pH 7.4, temperature = 37°C, PaO_2 = 40 mm Hg, respectively), indicating what percent of desaturation was solely due to PaO_2 changes. Furthermore, SaO_2 was calculated with PaO_2 remaining at each subjects' resting level, but with

pH, temperature, and $PaCO_2$ at their respective exercise levels, indicating what percent of desaturation was due to shifting of the oxygen disassociation curve.

Flow, volume, and pressure measurements. Inspiratory and expiratory flow was measured using independent pneumotachographs that were attached to a two-way non-rebreathing valve as described previously (14). Inspiratory and expiratory volume was obtained through numerical integration of the flow signal. Maximum expiratory flow–volume (MEFV) curves, EFL, and operational lung volumes were determined as previously described (11). To determine the onset and degree of EFL, we used the proximity of the tidal breath to the MEFV. Tidal breaths were placed within an MEFV that was obtained postexercise, which accounts for the effects of thoracic gas compression and bronchodilation on the assessment of EFL. Esophageal pressure was obtained by placing a 10-cm long latex balloon (no. 47-9005; Ackrad Laboratory, Cranford, NJ) ~45 cm down from the nostril after application of a topical anesthetic. Esophageal pressure was measured using calibrated piezoelectric pressure transducers (Raytech Instruments, Vancouver, BC, Canada). Using the flow, volume, and pressures obtained from several (6–12) breaths, the muscular work of breathing (15) and ventilatory capacity ($\dot{V}E_{CAP}$) were determined (21). We determined $\dot{V}E_{CAP}$ at rest and exercise using measured breathing parameters (duty cycle, tidal volume, and operational lung volume) and assumed that the subjects ventilated along their MEFV curve allowing for the determination of minimal expiratory time and subsequently maximal breathing frequency. Using the alveolar gas and ventilation equations with concurrent gas exchange measures, we estimated the $\dot{V}E$ required to increase PAO_2 sufficiently to return PaO_2 back to resting levels during each exercise stage. This information and $\dot{V}E_{CAP}$ assisted in determining whether it was mechanically possible for an athlete to normalize their blood gases by ventilating to a greater extent.

Data and statistical analysis. Raw data were recorded continuously at 400 Hz using a 16-channel analog-to-digital data acquisition system (PowerLab/16SP model ML 795; ADInstruments, Colorado Springs, CO) and stored on a computer for subsequent analysis (LabChart version 6.1.3; ADInstrument). Independent *t*-tests were used to compare subject characteristics between men and women, whereas a two-factor repeated-measures ANOVA was used to compare repeated measurements between men and women. A Tukey's HSD *post hoc* test was conducted when significant *F*-ratios were present. Pearson product–moment correlations were implemented to determine relationships between selected dependent variables. For all statistical comparisons, $P < 0.05$ was considered significant. Results are presented as mean ± SEM unless otherwise stated.

RESULTS

Physical characteristics and peak exercise data. Table 1 summarizes participant characteristics and pulmonary function data. The pulmonary function results are comparable with what is expected of young individuals free from pulmonary disease (16,26). Table 1 also shows cardiorespiratory values at peak exercise. Owing to the altitude of the testing facilities, the values for $\dot{V}O_2$ at maximal exercise were approximately 10% lower than would be expected at sea level (12). Several subjects had not used a treadmill previously. Familiarization trials were conducted, but we cannot exclude the possibility that lack of treadmill running experience coupled with the fact that subjects instrumented with invasive experimental apparatus may have induced some apprehension and precluded a true maximal volitional effort. In turn, these factors may have affected maximal O_2 consumption and minute ventilation values. Given the above, it is likely that some of our subjects did not achieve a true physiological maximum. We have adopted the term peak O_2 consumption ($\dot{V}O_{2peak}$) rather than $\dot{V}O_{2max}$.

TABLE 1. Subject characteristics and maximal exercise data.

	Males	Females
Age, yr	26.9 ± 1.3	21.0 ± 1.8*
Height, cm	172.7 ± 2.0	161.9 ± 3.0**
Mass, kg	54.8 ± 1.4	47.3 ± 0.4**
BMI, $kg \cdot m^{-2}$	18.4 ± 0.5	18.0 ± 0.1
BSA, m^2	1.65 ± 0.03	1.48 ± 0.01**
FVC, L	3.92 ± 0.17	2.66 ± 0.25**
FVC, % predicted[a]	109 ± 4	86 ± 6**
FVC, % predicted[b]	102 ± 4	77 ± 6**
$FEV_{1.0}$, L	3.20 ± 0.18	2.00 ± 0.27**
$FEV_{1.0}$, % predicted[a]	96 ± 5	72 ± 8*
$FEV_{1.0}$, % predicted[b]	87 ± 5	74 ± 9
FEV/FVC, %	81.6 ± 2.7	74.3 ± 4.2
MIP, cm H_2O	75.0 ± 7.0	62.1 ± 8.3
$\dot{V}O_2$, $mL \cdot kg^{-1} \cdot min^{-1}$	64.1 ± 1.7	49.5 ± 1.8***
$\dot{V}O_2$, $L \cdot min^{-1}$	3.50 ± 0.09	2.34 ± 0.08***
$\dot{V}CO_2$, $L \cdot min^{-1}$	3.55 ± 0.13	2.36 ± 0.13***
R	1.01 ± 0.02	1.01 ± 0.04
f_b, $breaths \cdot min^{-1}$	60 ± 4	54 ± 2
V_T, L	1.88 ± 0.09	1.39 ± 0.06**
f_H, $beats \cdot min^{-1}$	177 ± 4	181 ± 7
$\dot{V}E/\dot{V}O_2$	23.9 ± 0.7	23.9 ± 1.2
$\dot{V}E/\dot{V}CO_2$	23.7 ± 0.9	23.8 ± 1.1
ΔT_{EO}, °C	1.42 ± 0.16	0.85 ± 0.26
$\dot{V}E$, $L \cdot min^{-1}$	96.9 ± 3.7	64.7 ± 2.9***
$\dot{V}A$, $L \cdot min^{-1}$	79.9 ± 3.9	54.2 ± 7.7*
V_D/V_T	0.15 ± 0.01	0.17 ± 0.03
T_i, s	0.51 ± 0.03	0.57 ± 0.04
T_e, s	0.50 ± 0.03	0.60 ±0.06
T_{tot}, s	1.01 ± 0.06	1.16 ± 0.09
T_i/T_{tot}, %	51 ± 0.7	49 ± 0.9

Values are presented as mean ± SEM.
*$P < 0.05$, **$P < 0.01$, and ***$P < 0.001$ compared with males.
[a]Predicted values based on Kenyan normative data (26).
[b]Predicted values based on North American normative data (16).
BMI, body mass index; BSA, body surface area; FVC, forced vital capacity; $FEV_{1.0}$, forced expiratory volume in 1 s; MIP, maximal inspiratory pressure; $\dot{V}O_2$, rate of the volume of oxygen consumed; $\dot{V}CO_2$, rate of the volume of carbon dioxide produced; R, respiratory exchange ratio; f_b, breathing frequency; V_T, tidal volume; f_H, heart frequency; $\dot{V}E/\dot{V}O_2$, ventilatory equivalent for oxygen; $\dot{V}E/\dot{V}CO_2$, ventilatory equivalent for carbon dioxide; ΔT_{EO}, change in esophageal temperature from rest to maximal exercise; $\dot{V}E$, minute ventilation; $\dot{V}A$, alveolar ventilation; V_D/V_T, ratio of dead space volume to tidal volume; T_i, inspiratory time; T_e, expiratory time; T_{tot}, total time a breathing cycle; T_i/T_{tot}, inspiratory duty cycle.

Pulmonary gas exchange. Table 2 shows the mean values for arterial blood measurements at rest and during exercise. Values are reported for nine male and three female

TABLE 2. Arterial blood measurements at rest and peak exercise.

	Males		Females	
	Rest	Peak	Rest	Peak
PAO_2, mm Hg	84.5 ± 1.6	89.1 ± 1.1*	84.5 ± 1.3	88.2 ± 4.4*
PaO_2, mm Hg	78.8 ± 2.3	65.6 ± 1.5***	83.3 ± 0.6	71.5 ± 0.4***
A-aDO_2, mm Hg	5.7 ± 1.0	23.5 ± 1.7***	1.2 ± 1.4	16.7 ± 4.7***
SaO_2, %	96.5 ± 0.4	90.4 ± 1.7**	96.9 ± 0.3	93.3 ± 1.0**
$PaCO_2$, mm Hg	34.2 ± 0.9	33.6 ± 1.2	33.6 ± 1.9	34.3 ± 3.7
pH	7.42 ± 0.01	7.31 ± 0.03**	7.40 ± 0.02	7.33 ± 0.01**
Hb, $g \cdot dL^{-1}$	14.9 ± 0.4	15.7 ± 0.5**	13.4 ± 0.4	14.0 ± 0.4**
CaO_2, mL $O_2 \cdot dL^{-1}$	20.2 ± 0.6	19.9 ± 0.6	18.3 ± 0.6	18.4 ± 0.7
HCT, %	45.6 ± 1.3	48.1 ± 1.4**	41.2 ± 1.1	43.1 ± 1.2**
HCO_3^-, $mmol \cdot L^{-1}$	23.0 ± 0.4	18.1 ± 1.2**	21.9 ± 1.3	18.8 ± 1.0**

Values are presented as mean ± SEM.
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.
PAO_2, alveolar partial pressure for oxygen; PaO_2, arterial partial pressure for oxygen; A-aDO_2, alveolar to arterial difference in oxygen; SaO_2, arterial oxygen saturation; $PaCO_2$, arterial partial pressure for carbon dioxide; Hb, hemoglobin concentration; CaO_2, content of arterial oxygen; HCT, hematocrit; HCO_3^-, concentration of bicarbonate.

subjects due to failure to cannulate the radial artery in two subjects. There were significant reductions in PaO_2 and SaO_2 and a concurrent widening of the A-aDO_2 from rest to maximal exercise, but the differences were not different between men and women. Resting values for [Hb] and arterial O_2 content (CaO_2) were within the normal range, and exercise resulted in significant increases in hematocrit. Figures 1A–1D show the individual subject responses at rest and during progressive exercise for PaO_2, A-aDO_2, SaO_2, and $PaCO_2$, respectively. There was heterogeneity with respect to the temporal changes in gas exchange where some subjects exhibited reductions in PaO_2 (>10–15 mm Hg) at submaximal intensities, whereas others demonstrated hypoxemia only during heavy or maximal intensities.

Figure 2 shows the mean gas exchange values at rest and across all intensities of exercise. During submaximal exercise intensities, there were significant reductions in PaO_2 (>10 mm Hg) and SaO_2 (3%–4%) below resting values, which agrees with previously published definitions of EIAH (9). The reductions in SaO_2 and PaO_2 continued as exercise progressed. Decreases in SaO_2 were due to both decreases in PaO_2 and a shifting of the O_2–Hb dissociation curve due to exercise-induced hyperthermia and acidosis. Reductions in SaO_2 during submaximal exercise (<85% workload) were

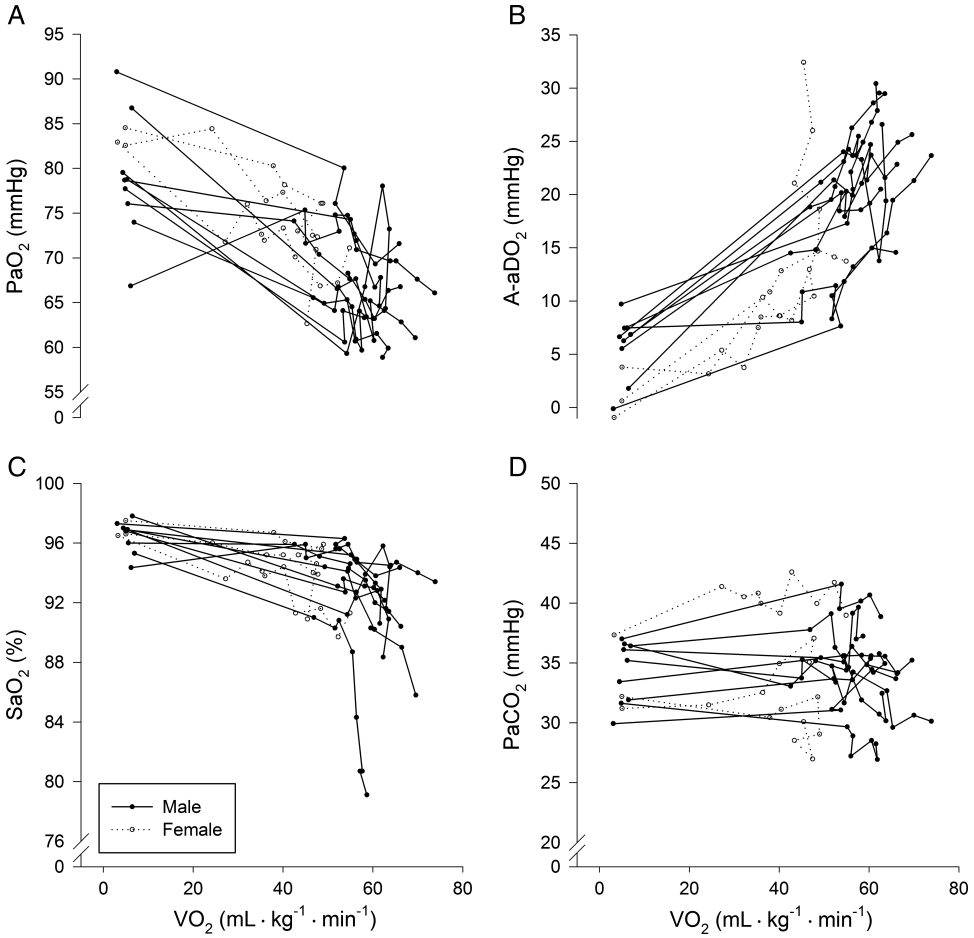

FIGURE 1—Individual blood gas values for individual subjects at rest and during incremental treadmill running to exhaustion. A, PaO_2, arterial partial pressure for oxygen. B, A-aDO_2, alveolar to arterial difference in oxygen. C, SaO_2, arterial oxygen saturation. D, $PaCO_2$, arterial partial pressure for carbon dioxide.

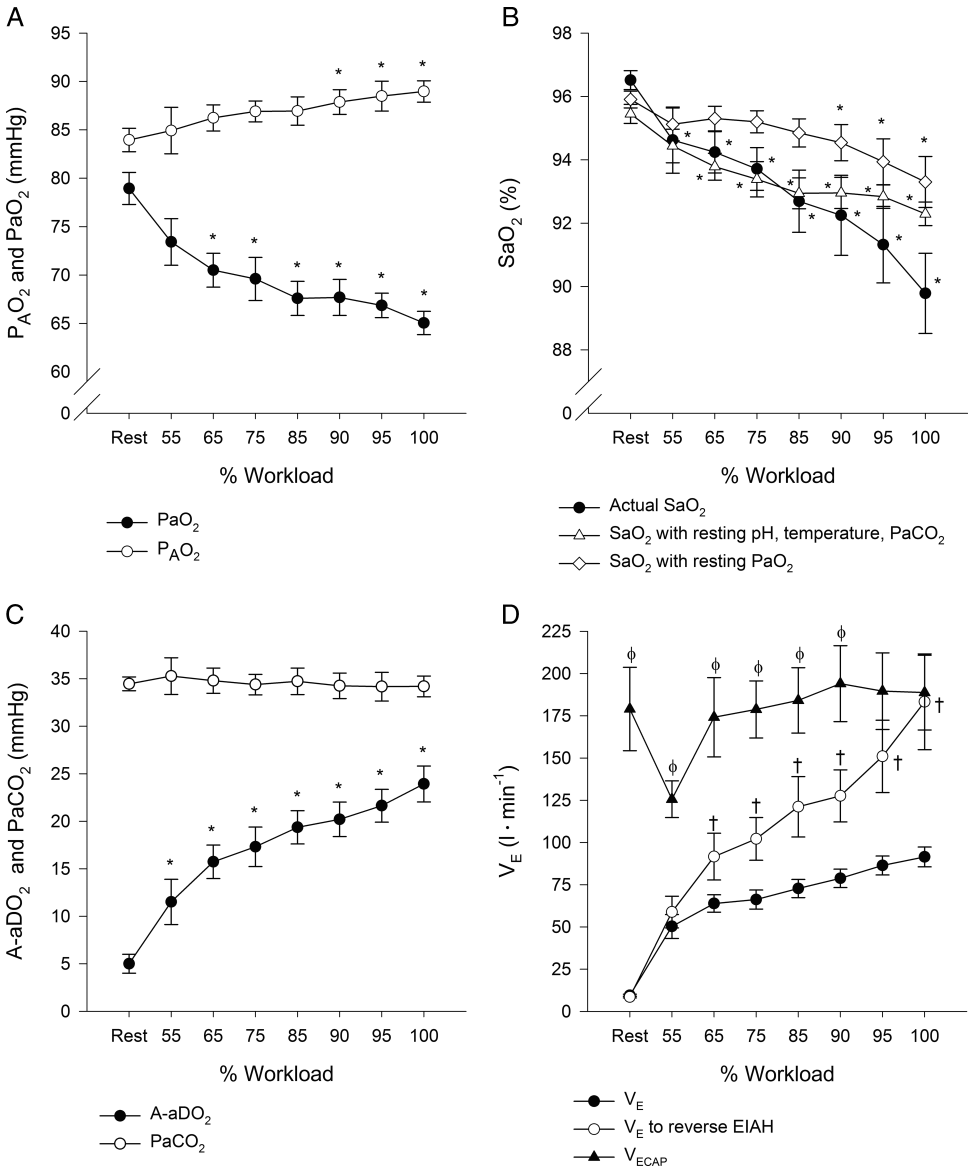

FIGURE 2—Arterial blood gas and minute ventilation values at rest and incremental percentages of maximal workload. A, PAO_2, alveolar partial pressure for oxygen and PaO_2, arterial partial pressure for oxygen. B, SaO_2, arterial oxygen saturation. Values for SaO_2 were determined in three ways: 1) direct measure from blood gas analyzer (*closed circles*), 2) calculated based on current PaO_2 applied to an ideal dissociation curve (pH 7.40, temperature = 37°C, $PaCO_2$ = 40 mm Hg) (*open triangles*), and 3) individual resting PaO_2 applied to a curve shifted due to current pH, temperature, and $PaCO_2$ (*open diamonds*). C, A-aDO_2, alveolar to arterial difference in oxygen and $PaCO_2$, arterial partial pressure for carbon dioxide. Values are presented as mean ± SEM calculated from both male and female subjects. *Significantly different from rest ($P < 0.05$). D, Measured expired minute ventilation (*closed circles*) and the $\dot{V}_E$ necessary to reverse exercise-induced arterial hypoxaemia (*open circles*). The ventilation necessary to raise PaO_2 back to resting levels was calculated using the alveolar gas and alveolar ventilation equations. Also shown is calculated ventilatory capacity ($\dot{V}E_{CAP}$, *closed triangles*). †Significantly different from $\dot{V}_E$ ($P < 0.05$). ϕSignificantly different from the $\dot{V}_E$ necessary to reverse EIAH ($P < 0.05$). At 55% workload, the $\dot{V}E_{CAP}$ was different owing to a brisk initial breathing response to exercise due to a relative tachypneic pattern and rapid decrease in end-expiratory lung volume. This tachypneic response involves a relatively small tidal volume, and the drop in EELV results in relatively smaller maximal flows due to the shape of the MEFV. As a result, the calculation of $\dot{V}E_{CAP}$ from the maximal expiratory flow volume relationship yields a decrease in $\dot{V}E_{CAP}$.

due to decreases in PaO_2, whereas during heavy exercise, further decreases in SaO_2 were principally due to acidosis and hyperthermia.

The A-aDO_2, or efficiency with which O_2 is exchanged between alveolar gas and arterial blood, continued to widen throughout exercise (Fig. 2C) and was highest at maximal intensity. There was a significant inverse relationship between A-aDO_2 and PaO_2 at peak exercise ($r = -0.73$, $P < 0.05$), whereas the relationship between PaO_2 and $PaCO_2$ was nonsignificant ($r = -0.42$, $P > 0.05$).

Figure 2D shows the changes in ventilation throughout the exercise test. As expected, $\dot{V}E$ increased progressively with exercise intensity while $\dot{V}E_{CAP}$ remained stable. The predicted ventilation that would be required to return PaO_2

to resting levels was significantly greater than the measured $\dot{V}_E$ from 65% of maximal workload onward and approached the $\dot{V}_{E_{CAP}}$ at 95%–100% maximal workload. As such, to eliminate EIAH via greater levels of hyperpnea, many subjects would have had to breathe at or even above their mechanically determined ventilatory capacity.

Expiratory flow limitation and work of breathing. Expiratory flow limitation was assessed in all 10 male subjects. During the final stage of exercise, two male subjects demonstrated significant flow limitation where the tidal breath intersected with the expiratory side of the maximum flow volume curve (22%–66%). No male subjects were flow-limited during submaximal exercise. Five of the other male subjects demonstrated "impending" EFL (23), where their tidal flow–volume loop approached the MEFV curve and developed its characteristic shape but did not fully intersect (see below). The female response was variable between subjects. Two female subjects exhibited flow limitation during the final stage of exercise, and one showed no flow limitation or impending flow limitation. The fourth subject was excluded from subsequent flow–volume analysis because of a failure to satisfactorily conduct the inspiratory capacity maneuvers.

Figure 3 shows an example of the responses to progressive exercise in one subject with impending flow limitation. Figure 3A shows resting and exercise tidal flow–volume loops plotted relative to the MEFV curve. Note that although true flow limitation is not present, end-expiratory lung volume approaches resting levels at maximal exercise, and the tidal flow–volume curve resemble the curvature to the MEFV loop. Shown in Figure 3B are tidal pressure-volume loops, which correspond to the same intensities as Figure 3A. On average, end-expiratory lung volume was not different from rest. The change in end-expiratory lung volume was variable among subjects where there were cases of appropriate reductions whereas there were also instances of relative hyperinflation.

Figure 3C shows the individual data points relating the mechanical work of breathing and $\dot{V}_E$ for men and women. Mean curves for men and women were constructed and are of increasing slope meaning that the mechanical work of breathing per any additional unit of air ventilated increased exponentially with increasing $\dot{V}_E$. To compare Kenyan and highly trained non-Kenyan runners, Figure 3C also shows the work of breathing values during incremental treadmill running from Johnson et al. (20). These values were selected because (i) subjects were on average of comparable aerobic fitness, and (ii) work of breathing measures was made across a range of ventilations such that curves could be constructed for comparative purposes.

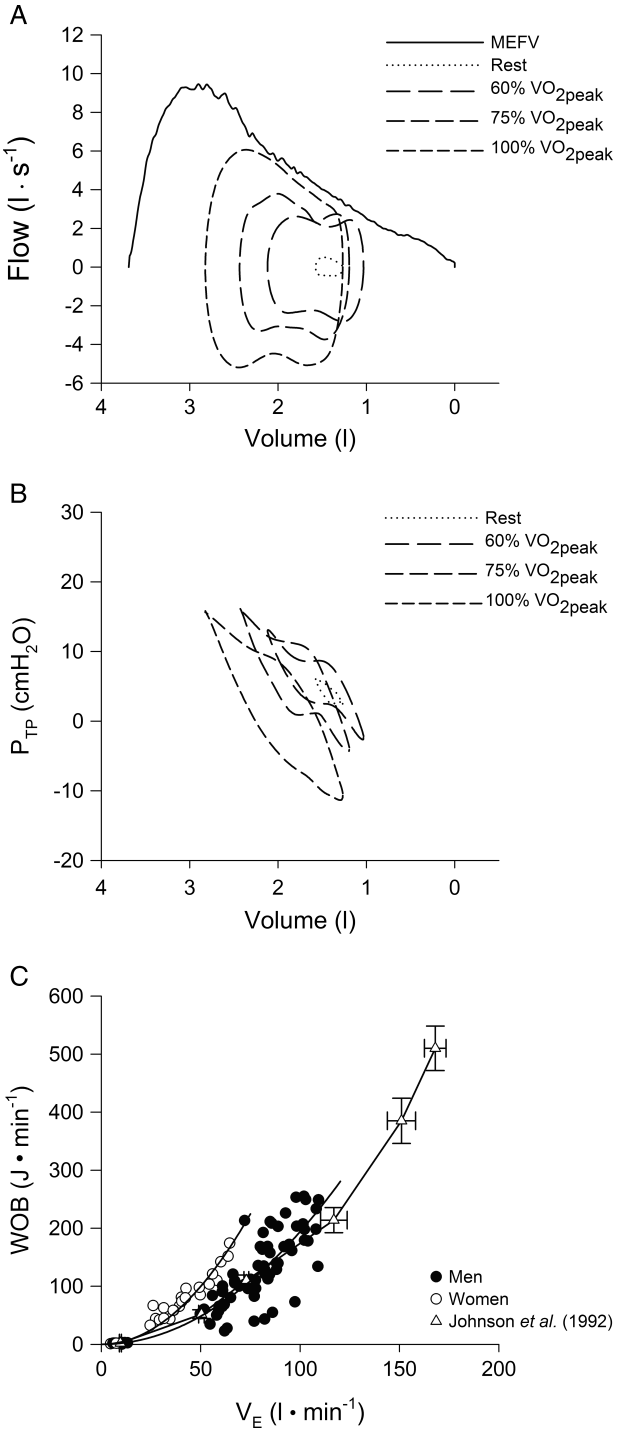

FIGURE 3—A, Mechanical work of breathing at different absolute minute ventilations. Shown are individual values for male and female subjects plotted against the range of ventilations obtained during exercise. Also shown are the mean work of breathing values from Johnson et al. (30). B, Representative maximal expiratory flow–volume curve and tidal flow–volume loops in a male subject at rest and during different percentages of peak oxygen consumption ($\dot{V}O_{2peak}$). MEFV, maximal expiratory flow–volume curve; PTP, transpulmonary pressure.

DISCUSSION

Main findings. This study was designed to systematically characterize pulmonary gas exchange and the mechanics of breathing during exercise in highly trained runners of Kenyan ancestry. We asked whether generational exposure to environmental hypoxia in conjunction with regular vigorous physical training might be of benefit such that the above-mentioned

pulmonary system limitations would be absent or minimal in Kenyan runners. Contrary to our hypothesis, we observed significant gas exchange impairments that would be of sufficient magnitude to compromise O_2 delivery. Furthermore, we found that runners from Kenya demonstrate EFL and high levels of respiratory muscle work that are commensurate with values seen in other aerobically trained athletes (20). The flow limitation we observed was of sufficient magnitude to limit ventilation from reaching the ventilation demanded during exercise. Our collective findings suggest that pulmonary system limitations are present in runners of Kenyan ancestry.

Pulmonary gas exchange. During incremental treadmill exercise, we observed significant reductions in PaO_2 and SaO_2 and a widening of the A-aDO_2. The fall in PaO_2 and SaO_2 began during submaximal exercise and worsened as exercise intensity increased. At peak exercise, the reduced SaO_2 was caused by a combination of reduced PaO_2 (~60%) along with acid shifts (~40%) in arterial blood and increases in core temperature. There were however notable between-subject differences in gas exchange during submaximal exercise where several subjects had reductions in PaO_2 during the initial treadmill stage whereas others maintained PaO_2 values close to resting levels (within 10 mm Hg) until near-maximal exercise intensity. We emphasize this observation because it is often underappreciated (8) that some endurance athletes develop substantial arterial hypoxemia during submaximal exercise. Reductions in arterial oxygenation may have multifactorial causes rather than a single cause (29), and the mechanisms responsible for submaximal EIAH are likely to differ from those at maximal exercise. Figure 2D displays the relationship between $\dot{V}_E$, $\dot{V}_{E_{CAP}}$, and the theoretical ventilation needed to offset the hypoxemia and raise PaO_2 to resting levels. However, we acknowledge that increasing $\dot{V}_E$ toward $\dot{V}_{E_{CAP}}$ would also lead to a significant reduction in $PaCO_2$ that could have deleterious effects itself. Throughout exercise, $\dot{V}_{E_{CAP}}$ remained stable, yet $\dot{V}_E$ and the theoretical $\dot{V}_E$ necessary to offset EIAH continued to increase and approaches $\dot{V}_{E_{CAP}}$. It is possible that tolerating submaximal EIAH may be a "strategy" to minimize respiratory effort and/or diaphragm and peripheral muscle fatigue as the $\dot{V}_E$ needed to offset EIAH would be considerable and result in a substantial work and O_2 cost of breathing (1). An excessive work of breathing and the ensuing fatigue of the respiratory musculature can lead to systemic deficits, such as decreased blood flow to peripheral muscles and muscular fatigue (17,30).

We observed a significant association between the A-aDO_2 and the PaO_2 at maximal exercise where those subjects with the greatest widening of A-aDO_2 had the greatest reduction in PaO_2 ($r = -0.73$, $P < 0.05$). Subjects in the present study exhibited EIAH owing to a combination of a widened A-aDO_2 and a blunted ventilatory response that was not sufficient to compensate for the excessive A-aDO_2. Several studies have used the multiple inert gas technique to show that ventilation–perfusion inequality contributes to the widened A-aDO_2 during exercise (13,29). A widened A-aDO_2 is also associated with end-capillary disequilibrium secondary to a high cardiac output and pulmonary blood flow leading to a shortened red cell transit time (7).

How does pulmonary gas exchange during heavy exercise in Kenyan runners compare with other runners of similar fitness? A difficulty here and the salient question is "What is the appropriate 'control' group?" To compare Kenyan runners born/raised at modestly high altitude, the comparative group must be fully acclimatized across physiological systems (e.g., ventilatory, hematological, metabolic, and cardiovascular). Moreover, the confounding issue of ancestral exposure to altitude needs to be considered. Despite the above caveats, some general comparisons can be made. The gas exchange impairments we report are consistent with other studies (9,18,20). Our values of A-aDO_2 as a function of $\dot{V}_{O_2}$ during heavy exercise are commensurate with compiled gas exchange data from previously published studies ($n = 57$ women, $\dot{V}O_{2max} = 32–70$ mL·kg^{-1}·min^{-1} and $n = 135$ men, $\dot{V}O_{2max} = 30–83$ mL·kg^{-1}·min^{-1}) (18). The exercise-induced reductions in SaO_2 and CaO_2 we observed are commensurate with what would be expected to reduce $\dot{V}O_{2max}$ and endurance performance and enhance the rate of development of peripheral muscle fatigue (30).

Respiratory mechanics. To assess the onset and degree of EFL during exercise, we placed tidal breaths within an MEFV curve that considered the effects of thoracic gas compression and bronchodilation (14). This is an important technical consideration as we were able to avoid overestimating the magnitude and incidence of flow limitation. We observed significant flow limitation during exercise in some but not all subjects during the final stage of exercise. Flow-limited subjects exhibited further increases in trans-pulmonary pressure without any increases in expiratory flow rate, which is the classic definition of flow limitation. In other instances, the maximal expiratory flow and pressure were achieved over only a portion of the V_T range at low lung volumes. This so-called "impending" flow limitation has significant importance with respect to the regulation of EELV and exercise hyperpnea (23). It has been argued that flow limitation and its compensatory responses (i.e., rise in EELV) should be considered on a continuum and dynamic rather than an all-or-none phenomenon (23). The onset of dynamic airway compression and the increases in airway resistance occur before expiratory flow becomes limited, and this likely has important consequences. As described by Babb (2), a minimal degree of EFL or approaching maximal expiratory flow likely alters breathing mechanics and contributes to breathing discomfort. In the present study, we observed an initial fall in EELV relative to rest in all subjects. The reduction in EELV below FRC during exercise serves to minimize the inspiratory elastic work of breathing and enables the diaphragm to operate near its optimal length for force generation (6). In this regard, it appears that Kenyan runners regulate EELV during submaximal exercise in the same way as other endurance trained athletes. During heavy exercise, we observed that, on average, EELV increased toward resting values and in many

instances EELV exceeded FRC. The rise in EELV during exercise has been associated with EFL, and that compression of the airways downstream from the flow limited segment may elicit a reflex mechanism that influences breathing pattern by prematurely terminating expiration (27). On the other hand, increases in EELV in the absence of EFL have been reported (24), suggesting that a reflexive mechanism to the change in EELV may be triggered even with impending flow limitation to avoid dynamic compression of the airways. In our study, the EELV response was variable between subjects and additional study is necessary before more generalized conclusions can be made.

Air density is reduced at high altitudes, which corresponds to a reduction in flow resistance. However, when at 3100 m (36), the work of breathing for a given O_2 consumption is higher. The reduction in airway resistance at high-altitude appears offset by the increasing turbulent flow produced by high flow air and increases in chest wall distortion. Although the altitude in our study was moderate, we cannot discount the possible effect a lower density of inspired gas has on our measures of breathing mechanics. With this in mind, the dynamic hyperinflation we observed is consistent with the concept that hyperinflation permits an increase in expiratory airflow at the expense of an increase in the elastic work of breathing because lung compliance is reduced at a high lung volume. It is known that hyperinflation can lead to early fatigue of the inspiratory muscles by requiring them to contract from a suboptimal length such that the muscular force necessary approaches the maximal force generating capacity (31). It is unknown if the diaphragm of maximally exercising Kenyan runners fatigues. However, many of the predisposing factors for fatigue of the diaphragm were present in our study, including EFL, a rise in EELV, a high work of breathing, and metabolic acidosis (19).

Critique of methods. First, native highlanders show larger lung capacities than do sea level residents. For example, larger lung capacities have been reported in high-altitude natives of Tibet and migrants to altitude only a few generations ago (4). Moreover, animal studies show that there is an effect of lifelong exposure on lung growth. In our study, we did not measure absolute lung volumes or pulmonary diffusion capacity. As such, we are unable to comment if Kenyan runners have an enlarged lung volume or higher lung diffusing capacity owing to their high-altitude ancestry. However, our spirometry values show no appreciable differences with predicted values. Second, we did not assess lactate during exercise. Rather, we made serial measures of arterial pH and bicarbonate, whole-body oxygen consumption, and carbon dioxide production during incremental exercise. The inclusion of lactate measures would have provided some additional insight into the metabolic responses to exercise as others have reported lower blood lactate values in Kenyan runners (33). Lastly, we did not determine the partial pressure of O_2 in the blood at which hemoglobin is 50% saturated (P50). There is some evidence that high-altitude populations exhibit an altered P50 (37) but relevant comparison with highly-trained acclimatized athletes are not available.

CONCLUSIONS

Which physiological factors explain the current domination of Kenyan and other East African runners in international competitions? There appears to be no marked differences in muscle morphology or metabolic profile between Kenyan and non-Kenyan athletes, nor is there a difference in $\dot{V}O_{2max}$ (32,33). In the present study, we found that pulmonary system limitations were present in Kenyan runners in the form of EIAH, EFL, and high levels of respiratory muscle work. This is consistent with what has been reported in other endurance-trained athletes. As such, it appears that Kenyan runners do not posses a pulmonary system that confers a physiological advantage.

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