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Commentaries on Viewpoint: The two-hour marathon: Who and when?

DON'T FORGET THE GUT—IT IS AN IMPORTANT ATHLETIC ORGAN!

TO THE EDITOR: It was with great interest that we read the *Journal of Applied Physiology* Viewpoint on the 2-h marathon barrier (3). We would argue that, alongside having a superlative $\dot{V}O_{2max}$, lactate threshold, and running economy, it will be required for this athlete to have an individualized and aggressive fueling strategy coupled with a predisposition for high exogenous CHO oxidation (CHO_{exog}), without a history of GI distress. It is clear that supplemented carbohydrate (CHO) improves prolonged endurance performance (>90 min) compared with water (2). Furthermore, recent evidence has demonstrated a positive dose-response relationship between supplemented CHO, CHO_{exog}, and endurance performance; where 60 g CHO/h outperformed either 15 or 30 g CHO/h (5). The maximal CHO_{exog} with single CHO sources appears to be ~1 g/min due to limitations of the intestinal transporters (1). However, despite any individual differences in CHO_{exog} or history of GI distress (4), CHO_{exog} is not dependent on body weight (BW), as a recent analysis has shown no relationship between BW and CHO_{exog} (1). Accordingly, a 56-kg runner is able to oxidize ~20% more per kg BW compared with a 70-kg runner with a given CHO_{exog} rate of ~1 g/min (1.07 vs.0.86 g $CHO \cdot h^{-1} \cdot kg\ BW^{-1}$). Therefore, there appears to be a distinct CHO_{exog} advantage for lighter marathon runners compared with heavier. Thus the future 2-h marathon runner will feature a low BW, *both* for improved thermoregulation, but also optimal CHO_{exog} per kg BW. *All* of these elements will need to be possessed by the first athlete to break the 2-h marathon barrier.

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MARATHON RUN IS AN IMPORTANT STRESS TO MUSCLE AND BRAIN FUNCTIONS

TO THE EDITOR: In their Viewpoint, Joyner, Ruiz, and Lucia (2) specifically highlight the important role of "exceptional running economy" as one of the main physiological factors for breaking 2 h for a marathon run. We totally agree that future studies should investigate not only mechanical factors related to running economy, but also the complex links between heat storage, body size, and functional links between muscle and brain with fatigue. First, as a plausible source of "exceptional running economy" there are some favorable types of runner's footstrike patterns. Recent detailed analyses of foot kinematics and kinetics in barefoot and shod Kalenjin runners (2) corroborate and extend what is known about the mechanics of barefoot running (3). So, fore-foot striking runners are prompt to take further advantage of elastic energy storage in both the Achilles tendon and the longitudinal arch of the foot. Second, one possible issue is that athletes (African vs. white runners) pace themselves differently during marathon in hot conditions (4), and the rate of heat storage is a likely candidate that mediates this difference. Part of this difference is the larger body size of the white runners, suggesting that their rate of heat storage would be higher than the African runners at the same speed. Third, the breakdown of running style over the distance suggests that muscles are no longer activated ideally and ultimately central nervous system is affected by long-lasting exercise (5) associated with increased temperature. Each of these factors can play a significant role in aerobic exercise performance.

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WEALTH AND ATHLETIC RECORDS

TO THE EDITOR: Improvements in athletic performance (4) have long fascinated investigators (3). The plot against time is relatively linear, but breaks in this trajectory arise from factors such as new technology or doping. Possible developments in marathon running include shoes designed to return elastic energy, high-altitude training, and blood doping, all more likely available to contestants from wealthy nations.

An important cause of the underlying trend is a progressively more complete search of world populations for optimal phenotypes. To date, this search has probably been less exhaustive in developing nations such as Kenya than in countries that make major investments in international competition.

Physiological advantages in addition to a large maximal oxygen intake and a high mechanical efficiency include the ability to exercise for long periods at close to maximal oxygen intake (2)—probably an expression of both motivation and the percentage of Type I muscle fibers—and a concentration of muscle mass in the active limbs. Loss of protein from other parts of the body during training is diminished by glycogen loading (1) and a high protein intake, more likely among competitors from wealthy nations. It would be interesting to compare the ratio of leg to whole body mass among runners from various nations, but I suspect such ratios would be highest in those from the third world.

"Who" breaches the 2-h barrier may thus depend on the relative importance of factors associated with affluence and those linked to limited material resources.

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MATURITY EFFECT OF TRAINING

TO THE EDITOR: Joyner, Ruiz, and Lucia (4) bring up interesting and thought-provoking concepts in their Viewpoint on the possibility of the 2-h marathon. However, one factor that was perhaps overlooked is the effects of maturity and time in developing the marathon runner. Joyner and Coyle (3) have said that the "outcome of all Olympic endurance events is decided at intensities above 85% $\dot{V}O_{2max}$ and most require athletes to be relatively fatigue resistant at intensities that stimulate significant anaerobic metabolism." The improvements made in economy with maturity of the athlete in a training program should not be overlooked, as they allow athletes to operate at higher percentages of their $\dot{V}O_{2max}$ and lactate thresholds for longer periods of time. Jones (4) showed that 9 yr of training led to a 15% improvement in economy (from 205 $ml \cdot kg^{-1} \cdot min^{-1}$ to 175 $ml \cdot kg^{-1} \cdot min^{-1}$ at 16 km/h) while $\dot{V}O_{2max}$ remained relatively constant. Similarly, Coyle (1) showed an 8% improvement in muscular efficiency after 7 yr of training, where the athlete improved his power output at ~83% of his $\dot{V}O_{2max}$ (~5 l/min) to 403 W from 374 W.

The maturity of an athlete under the guidance of a well-structured training program warrants further investigation, as it is logical to think the current or next world record holder in the 10,000-m run or half-marathon may take a minimum of 10 yr to reach their potential peak fitness for the marathon distance *after* setting their record, as Gebrselassie did (1998: 10,000 m, 26:22; 2008 marathon 2:03:59).

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MECHANISMS OF SELF-OPTIMIZED PACING

TO THE EDITOR: In sport, breaking barriers cause athletes and coaches to enter history and scientists to think deeper to the limits of human beings. In men's marathon, the last frontier was the 20 km/h pace (3:00 per km) on 20 September 1998 in Berlin (2h06:05) by the Brazilian runner Ronaldo Da Costa coached by the legendary Carlos Cavalheiro. This is still the fastest time ever run by a non-African born athlete (3)!!

It is known that marathons are not run at a constant pace (for example, Da Costa had a negative split of 1:04:42 first half, and 1:01:23 second half, whereas Gebrselassie ran between 2:58.2 and 2:53.8 per km for the current World record, 2h03:59) and that constant pacing is more stressful than self-pacing (4). So, beyond economy, $\dot{V}O_{2max}$ and the other classically described parameters, e.g., lactate threshold or fraction of $\dot{V}O_{2max}$; storage-recoil of elastic energy in muscle-tendon units; heat dissipation capacity and their morphological attributes; the ability to adjust adequately the pacing is emerging as another factor of importance (6).

In our view, two potential mechanisms of pacing self-optimization require further interest. First, the vertical and leg stiffness changes under fatigue have not been studied for durations longer than 1 h (2). Second, the kinetics of $\dot{V}O_2$, specific to each activity (5) is proposed as a key determinant of endurance performance (1).

These two mechanisms are under the influence of the slight changes in velocity during the marathon but we don't know if/how they interact with the energy cost. However, one may postulate that they might help us better understand how a runner will grab the few seconds that are still missing to the 2-h record.

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IMPLICATIONS OF THE CRITICAL SPEED AND SLOW COMPONENT OF $\dot{V}O_2$ FOR THE 2-HOUR MARATHON

TO THE EDITOR: The "two-hour marathon barrier" discussed by Joyner et al. (3) presents an interesting physiological conundrum. We believe it is instructive to consider the problem in light of the contemporary paradigm of $\dot{V}O_2$ kinetics (1) and the critical power/speed model (for review, see Ref. 2).

For running, the "heavy" exercise domain is bounded by the lactate threshold (LT) below and the critical speed (CS) above. It is characterized by the appearance of a slow component of $\dot{V}O_2$, which increases the energetic cost of exercise despite a constant work rate (1, 4, 5). This phenomenon has been the source of much debate, but the emerging consensus view is that it reflects the recruitment of higher order (type II) muscle fibers, which have different metabolic properties (4, 5). Above CS, there is an additional disturbance of metabolic homeostasis [i.e., inability to stabilize $\dot{V}O_2$, creatine phosphate (PCr) levels, pH, etc.], and the finite, chiefly anaerobic, work capacity (W′) will be expended at a predictable rate; once the W′ is depleted, the athlete will fatigue, necessitating a reduction in running speed (2).

Given that any future 2-h marathon will be completed within the heavy exercise domain, we would expect that the athlete breaking the 2-h barrier will exhibit a relatively high CS-to-body mass ratio, coupled with a relatively small slow component. These factors are likely more important for success than the absolute $\dot{V}O_{2max}$ (which the athlete cannot closely approach) or running economy (measured in the moderate exercise domain) per se.

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THE 2-H MARATHON—RUNNING FROM EAST

TO THE EDITOR: In their Viewpoint, Joyner, Ruiz, and Lucia (3) make interesting speculations about who and when will run a 2-h marathon; some cardiovascular pathophysiological considerations could help to better delineate their profile of a perfect runner. Authors identify some features associated to good long-distance running performances: birth on uplands, small body size, and exercise habit since childhood. They claim that genetic pulmonary adaptation to high altitude reduces arterial desaturation during heavy exercise and predisposes to good endurance performances. In effect, it is well known that natural selection, operated by exposure to hypoxic environments since prehistoric times, induced remarkably high maximal oxygen consumption in natives of high altitudes (1). On the other hand, a reduced alveolar ppO_2 also induces pulmonary vasoconstriction and hypertension that is considered a nonadaptive epiphenomenon and that could limit highlanders' physical performances (4). A remarkable exception exists: normal resting pulmonary arterial pressure and low pulmonary pressure response to exercise (2) have been reported in Tibet natives (people with the oldest altitude ancestry in the world and with a virtually complete evolutionary adaptation to chronic hypoxia). At present, athletes from Tibet are not used to compete in marathon (possibly due to cultural or political reasons), but in the future they could. The above reported considerations suggest they perhaps represent the ideal marathon runners. The perfect runner could thus come from Asia and, may be, in a courtyard of Lhasa, a young Lama is now playing with the future 2-h marathon winner.

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THE TWO-HOUR MARATHON—WHO AND WHEN? AND IN WHAT ENVIRONMENTAL CONDITIONS?

TO THE EDITOR: The interesting paper of Joyner et al. (5) attempts to identify the physiological characteristics of the individual who could break the 2-h barrier in the marathon foot race (42 km). An essential addition to this work should be the inclusion of compulsory environmental conditions needed to accomplish this feat, as the environment imposes limits to endurance performance (1).

The ambient temperature range most conducive to fast marathon times is 10–12°C (50–54°F; Ref. 2) and recent research has documented that with increasing heat stress there is a progressive and quantifiable slowing of marathon performance (3). A common trait of fast marathon performers is the ability to maintain a constant running velocity (4). As environmental temperatures increase, it is the fastest runners who are unable to maintain their pacing strategy and suffer the greatest deceleration in their running velocity profile (4).

Ambient temperature is the primary environmental determinant of a fast marathon performance as cloud cover and solar load appear to have little influence (2). Additionally, "humidity" does not appear to be a factor as marathons are usually contested at relatively cool temperatures where skin temperatures and water vapor pressures are both low.

An individual must therefore not only be blessed with the physiology of a high $\dot{V}O_{2max}$, lactate threshold, and running economy (5), but also with near ideal (10–12°C; Ref. 2) temperature conditions on race day if the 2-h threshold is ever to be broken.

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THE 2-HOUR MARATHON—MORE THAN PHYSIOLOGY

TO THE EDITOR: Joyner et al. (2) write an excellent Viewpoint discussing the combination of factors such as running economy, body weight, maximal aerobic capacity, and genetics that may ultimately lead an individual to break 2 h in the marathon. However, the discussion cannot be complete without consideration of (at least) two additional factors: psychology and opportunity. Elite marathoners have a unique psychological profile: they are emotionally stable, highly motivated, driven by intrinsic rewards, and possess strong psychic vigor (3, 4). Moreover, these traits are innate rather than acquired, indicating that this psychological profile predisposes the individual to achieve success at the elite level. Therefore, it is highly likely that the marathoner who eventually dips under the 2-h barrier will possess a winning combination of both physiological and psychological attributes. In addition, the individual who possesses the genetic, physical, and mental proclivity to run the sub-2-h marathon must also be the individual who is given the opportunity to do so. The author Malcolm Gladwell, in his book *Outliers*, concludes that the accomplishments of extremely successful people are attributable at least in part to the contributions of many different resources. In other words, extraordinary outliers are an amalgamation of the talented individual with his or her culture, community, family, and environment that together create a unique opportunity to succeed. Therefore, the runner who ultimately finishes the marathon under 2 h must first be given the opportunity (through exposure, financial resources, optimal training, social support, etc.) to start.

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THE 2-HOUR MARATHON: OLYMPIAN VS. PARALYMPIAN

TO THE EDITOR: We agree that $\dot{V}O_{2max}$, lactate threshold, and running economy are physiological determinants of distance running performance (1, 2) as discussed by Joyner et al. (3). We would like to share two additional assertions. First, due to ongoing controversy regarding whether a bilateral transtibial amputee wearing prostheses could and/or should compete in the Olympics, that any distinction between physiological and biomechanical influences on performance is blurred, and second, that clear performance-based distinctions between "able-bodied" and "disabled" athletes may likewise become increasingly problematic.

South African track athlete Oscar Pistorius' world-record runs of 10.91 s in the 100 m, 21.58 s in the 200 m, and 46.56 in the 400 m are both inspiring and provocative. Although these times are not as fast as the world-record times for "able-bodied" athletes (9.58 s in the 100 m, 19.19 s in the 200 m, Usain Bolt; 43.18 s in the 400 m, Michael Johnson), Pistorius may qualify for the 2012 London Summer Olympics. What if he was a distance runner? Based on the Viewpoint, the question is: What if a bilateral amputee became a gifted marathoner, wearing the same high-tech J-shaped carbon-fiber prosthetics ("blades") worn by Pistorius? Haile Gebrselassie's current world record for the marathon is 2:03:59. If his metabolic cost of running was reduced by 3.8% (4), and if this corresponded to a concomitant time reduction, then he could hypothetically run a 1:59:16. Whether or not the time would be recognized by a sanctioning body, this point must be recognized: the first person to run a marathon in under 2 h may not be an Olympian, but a Paralympian.

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THE 2-HOUR MARATHON: WILL WOMEN CLOSE THE GAP ON MEN?

TO THE EDITOR: In their Viewpoint, authors raise an interesting question about when the 2-h marathon barrier will be achieved and by whom (2). One important point that should be taken into consideration is whether sex will matter in the long run. Speculations among scientists regarding the sprinters running the Olympic 100-m sprint race suggest that women's performance is improving faster, allowing them to narrow the gap on men (1, 4). Some investigators suggest that women sprinters may overtake the world record and become faster than men in 150 yr or so from now (4). Over the longer distances, such as the marathon, the rate of improvement of the women has been even faster (3), suggesting that, although men might be able to break the 2-h psychological barrier for the marathon earlier than women, women marathoners might finally close the gap and overtake men in the long run.

Against those speculations is the fact that men and women are fundamentally different in their physiology and build. For example, men have at least 10 times more circulating testosterone than women, which boosts muscle power and oxygen capacity in men naturally (5). With such innate advantages of being a male athlete, it seems difficult to see how female athletes could ever catch up with the performance of men. Whether these narrowing trends will continue over time, reach a plateau, or even become wider remains to be seen.

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FEASIBLITY OF THE TWO-HOUR MARATHON IS A BURNING ISSUE

TO THE EDITOR: Calculations show that athletes with feasible metabolic capabilities could complete a marathon in 2 h (4), clearly a phenomenal performance. Elite distance runners have exceptional economies, but most estimates ignore that economy deteriorates during the event, and these estimates are expressed as oxygen uptake (3), rather than the more relevant energy equivalent (2). An average energy cost throughout the marathon of 4.18 $kJ \cdot km^{-1} \cdot kg^{-1}$ is a reasonable and conservative estimate. Assuming an efficiency of zero (level grade locomotion has no net work), 9.87 MJ of heat is generated for a 56-kg runner, corresponding to a 1°/km temperature gain. Heat loss by evaporation would require ~4.5 liters of sweat. This might seem feasible too, but keep in mind we are dealing with a 56-kg athlete, and not all of the sweat would evaporate! A loss of 1.2 kg would correspond to a 2% mass loss; performance would deteriorate (1). They would have to drink over 3.3 liters during the 2 h to prevent this. Of course, a high body surface area-to-mass ratio will help conductive and convective heat dissipation, so this 4.5 liters is an overestimate. It may be that the runner who breaks this 2-h barrier will have exceptional skin blood flow and a very high body surface area-to-mass ratio (5). The truth is that to provide an accurate description of the physiological capabilities of this superb athlete, we will have to obtain more detailed measurements of the current record level athletes.

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THE TWO-HOUR MARATHON: HOW IMPORTANT IS AGE?

TO THE EDITOR: Age could be a key characteristic of the runner who will break the 2-h marathon. How old will this runner be? The average age of the elite marathon runner is 28.9 ± 3.8 yr for men and 29.8 ± 4.2 yr for women and this age has not systematically altered in the last 10–20 yr (2). Haile Gebrselassie was 35 yr when he set the current world record for the men's marathon (2008) and Paula Radcliffe was 29 yr when she set the record for women (2003). $\dot{V}O_{2max}$ and running economy are important factors contributing to marathon performance (3), but age appears to affect these factors differently. The primary mechanism mediating the age-related decline in $\dot{V}O_{2max}$ is maximal heart rate (5), which declines from 20 to 25 yr (1, 4). Reductions in marathon performance, however, occurs from 35 yr of age (5). In contrast to $\dot{V}O_{2max}$, running economy can improve dramatically for a runner over the years (3). Consequently, improved running economy is important (3) and may offset the inevitable age-related decline in $\dot{V}O_{2max}$, at least for up to 10 yr to improve or maintain running performance. Exceptional running economy therefore, may explain why the marathon world record holders were not 20 or 25 yr of age. The implications are that whoever breaks the 2-h marathon may be a younger runner who is already endowed with an exceptional running economy and can therefore take advantage of a $\dot{V}O_{2max}$ that has not begun the inevitable age-related decline.

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THE TWO-HOUR MARATHON: THROUGH A HIGHLY INDIVIDUALIZED TRAINING PROCESS?

TO THE EDITOR: It is clear that only a genetically gifted runner (3) would break the 2-h marathon record. Nevertheless, since training responses are remarkably individual (5) and since the runner's potential has to be most favorable come D day, the tight individualization of training *1*) orientation, *2*) content, and *3*) periodization are also important factors toward the success of breaking this record.

1) Anthropometric, cardiovascular, neuromuscular, and biomechanical profiling to target middle-to-long-term training orientations and priorities.

2) Providing key reference running speeds that are associated with specific training-induced adaptations (4). While high-intensity sessions performed near the velocity associated with $\dot{V}O_{2max}$ elicit both central and peripheral adaptations, low-intensity and long sessions run below the first ventilatory threshold serve to signal the aerobic phenotype and promote physiological recovery (4). The velocity associated with maximal fat oxidation rate or larger stroke volume can target body fat loss or myocardium morphological adaptation, respectively.

3) Monitoring changes in cardiovascular autonomic control [via heart rate variability (HRV) measures] to assess training effectiveness and a runner's readiness to perform. HRV is likely one of the most promising tools, providing an instantaneous insight into both acute and long-term individual responses/adaptations to aerobic training (2). For instance, training-induced changes in HRV can predict improvements in distance running performance (1) and can serve to adjust (and therefore individualize) training content on a daily basis, leading, in turn, to greater improvements in running performance (2).

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WHAT FOR NATURE, AND WHO TO NURTURE?

TO THE EDITOR: The perspective of Joyner et al. (4) presents several intriguing hypotheses concerning the physiological characteristics of the first sub-2-h marathoner. Our interests lie in long-term maturation of these characteristics and how such maturation may impact prediction of who will break the 2-h barrier.

Longitudinal designs are heavily outweighed by cross-sectional studies of performance physiology, and we know only two investigations that have followed "world-best" endurance athletes (2, 3). These studies of a world record marathoner and multiple Tour de France champion both indicate that improved economy contributes to long-term improvements in performance, while maximal oxygen consumption ($\dot{V}O_{2max}$) either decreases or remains unchanged. This suggests that physiological maturation favors economy over $\dot{V}O_{2max}$. As such, future world-best performers are more likely to undergo long-term improvement in economy than $\dot{V}O_{2max}$, but candidates for the first sub-2-h marathoner will exhibit exceptional $\dot{V}O_{2max}$ at a young age.

To support this logic with performance metrics, both current marathon world record holders began their careers as outstanding performers over shorter distances [which typically require higher $\dot{V}O_{2max}$ (5)]. Gebrselassie's early marks still rank him in the two fastest of all time over distances from 3,000 m through the marathon, an exceptional range (1). Among younger runners, Kenenisa Bekele exhibits similar early career success, and presuming that he matures comparably to Gebrselassie, an unsophisticated extrapolation of the difference between their 10,000 m records suggests a marathon time of ~2:02:13.

Our perspective contends that maturational improvement in economy will contribute to determination of the first 2-h marathoner. We encourage publication of further longitudinal data, which surely exist, to better describe physiological maturation in elite endurance athletes.

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PHYSIOLOGICAL DETERMINANTS OF BEST PERFORMANCE IN MARATHON RUNNING

TO THE EDITOR: In their Viewpoint, the authors (1) predict the improvement in marathon times on the basis of a linear extrapolation of marathon best performances over the last 50 yr. They suggest that within 12–13 yr, marathon runners may break the 2:00-h limit. However, any running record prediction made on the basis of linear extrapolations may be fallacious and has been criticized on several grounds (3). The knowledge of the physiological determinants of best performances in human locomotion is required when predictions are to be made (4). In the context of endurance running, the speed maintained during the race (v, m/s) is equal to the ratio between the aerobic metabolic power (fraction of the $\dot{V}O_{2max}$ used during event, F, times $\dot{V}O_{2max}$, W/kg) and the energy cost of locomotion (C, J/m kg) (4). For instance, athletes like those studied by Larsen (2) ($\dot{V}O_{2max}$: 28.6–29.3 W/kg, C: 3.9 J/m kg) would need an F value of 0.78–0.80 to run a marathon in 2:00 h (5.9 m/s). Therefore, we cannot exclude that an athlete endowed by the combination of a high $\dot{V}O_{2max}$ and a low C may break this remarkable limit well before the time predicted by the authors.

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INFLUENCE OF EARLY LIFE FACTORS ON ELITE PERFORMANCE

TO THE EDITOR: The Viewpoint by Joyner and colleagues (3) introduces the connection between early life factors and elite performance that, unfortunately, has not yet received much attention. Our biology is subject to considerable plasticity during early life. Potent prenatal stimuli can contribute to prolonged functional and metabolic changes that can lead to physiological programming of the offspring (2). Prenatal exposure to high altitude generates vascular adjustments resulting in increased uterine artery oxygen delivery, particularly in highlanders (4). This adaptation exerts a strong influence on cardiopulmonary function that may reduce the incidence of arterial desaturation observed during heavy exercise in elite athletes. Indeed, the birthplace of the current top 13 marathoners, and the vast majority of the top 50, was above 1,500 m. Moreover, early life physical activity, a common feature of East African life, contributes to increased skeletal muscle mass, left ventricular mass, myofibrillar protein, motor coordination, and reduced inflammatory cytokine levels during adulthood (1, 5). It is likely that in East Africa these early life factors collide with a genetic advantage to induce biological changes that may allow for a more robust training response in adulthood. Indeed, East Africans' slimmer lower legs and high capacity for fatty oxidation have tremendous impact on running economy and performance. Yet, the evidence supporting a genetic advantage in marathon performance remains weak, highlighting the strong influence of early life factors on elite performance. Further investigation of these factors through novel approaches combined with genomic technologies, will provide insight on "who" will break the 2-h marathon barrier.

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TWO-HOUR MARATHON: BAYES TAKES A DAY OFF?

TO THE EDITOR: Joyner et al.'s Viewpoint luxuriates in using fastest times (i.e., best case scenario) to predict sub-2-h marathon performance (2). Yet, if Thomas Bayes were allowed into the conversation, one would question not "when," but "if" it is even feasible. By taking the top 500 men's marathon performances of all time (range 02:03:59–02:08:42), examining annual rates of improvement (AROI) for mean and the distribution range (fastest vs. "slowest") of progressions, the estimated likelihood of sub-2-h becomes questionable. Using all men's performances regardless of nationality the AROI (years until a sub-2-h) is: fastest [9 s/yr (27/yr)], slowest [1 s/yr (240 yr)], and mean [2 sec/yr (120 yr)]. When considering just the Kenyans who own 252 of the top 500 times the AROI are: fastest [9 s/yr (27 yr)], slowest [1 s/yr (240 yr)] and mean [5 s/yr (48 yr)]. For the Ethiopians, holders of 59 of the fastest times, the AROI are: fastest [16 s/yr (15 yr)], slowest [0 s/yr (*never*)], and mean [5 s (48 yr)]. More sophisticated models further suggest a limit to human marathon performance in men (02:03:59 vs. 02:03:08, time gap 51 s) and women (02:15:25 vs. 02:13:30, time gap 115 s) for current vs. predicted times, respectively (1). Not discounting "outlier performances," such as Haile Gebrselassie's 2008 Berlin performance that eclipsed the previous fastest time by 27 s, different analytic techniques imply that such a feat ranges from "soon" (~15 yr), to "a long time" (~240 y), to *never*. Nonetheless, the topic does make for good discussion.

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THE TWO-HOUR MARATHON: RUNNING ECONOMY AND LOWER BODY FLEXIBILITY

TO THE EDITOR: The Viewpoint by Joyner et al. (4) regarding the "two-hour marathon" highlights an interesting area of human performance, one involving physiological, genetic, nutritional, social, and psychological aspects. Running economy, known to be an important factor affecting elite marathon performance as well as $\dot{V}O_{2max}$ and lactate threshold (2), is influenced by lower body flexibility.

Running economy is significantly correlated with lower body flexibility when tested using the sit-and-reach test (2, 5) and dorsiflexion and standing hip rotation measures (1) in international-standard (2), sub-elite (1), and collegiate (5) distance runners. This negative relationship is likely due to increased storage and return of elastic energy in stiffer musculotendinous structures during the stretch-shortening cycle, which reduces the aerobic demand of submaximal running. Body heat generation is also minimized by rapid and efficient reutilization of this stored energy. In other words, less flexible runners are more economical.

In addition, running economy appears significantly related to ankle range of motion tested with a straight leg (stretching soleus, gastrocnemius, and hamstrings) but not a flexed leg (stretching soleus only) in university-standard distance runners (unpublished observations, Drew and White, 2004). This could suggest that soleus muscle length is not a limiting factor of running economy. Rather, less flexibility in the gastrocnemius, hamstrings, hip joint, and/or lower back area may have more of an influence on the oxygen cost of submaximal running.

Therefore, whoever breaks the 2-h marathon record may have relatively stiff musculotendinous structures in their lower body, which may contribute to their exceptional running economy.

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IS THE MEN'S MARATHON WORLD RECORD 25 YEARS BEHIND THE WOMEN'S RECORD?

TO THE EDITOR: Joyner et al. (3) predict a 2-h marathon may occur within ~25 yr (3). There is no doubt this would be an impressive physiological feat, but we wonder how impressive this really is in the context of the current women's world record of 2:15:25 set by Paula Radcliff. A 2:00:00 hour men's marathon is equivalent to 2:15:34 for women according to the Mercier scoring system; a time that has already been beat by Radcliff 7 yr ago. The Mercier scoring system is a statistical cross-event performance comparison tool, based on average running velocity (Vavg) obtained from weighted world rankings over four consecutive years (1995–1998). The Vavg for 5th, 10th, 20th, 50th, and 100th ranked performances in each event are assigned a common point score and fit via linear regression ($r^2 > 0.99$ for most events).

Possible sex differences in substrate utilization (5), muscle fiber type characteristics (4), and the consistent finding of greater skeletal muscle fatigue resistance in women (1, 2) may explain, in part, why the performance gap between sexes is lowest for the marathon compared with every other distance in athletics. To break 2:00:00 would require a 3.21% reduction in the current men's record. An equivalent drop in the women's record would bring Radcliff's time down to a staggering 2:11:04. Given that women are, on a relative basis, well ahead of men in the marathon, we would safely bet that we will see a 2:00:00 h men's marathon well before we see a 2:11:00 marathon in women.

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ROLE OF ALTITUDE TRAINING AND THE TWO-HOUR MARATHON

TO THE EDITOR: In asking "What will the two-hour marathoner look like," Joyner and colleagues (3) suggest that exposure to high altitude early in life may play a role, perhaps by minimizing pulmonary gas exchange limitations during exercise. We agree that altitude will almost certainly have to play a prominent role if 2 h is to be broken in the marathon, but rather via a different mechanism of maximizing red cell mass and improving the $\dot{V}O_2$ at the ventilatory threshold/maximal steady state.

Joyner's (2) previously published mathematical model for optimal marathon performance in "ideal" weather and course conditions indicates three physiological components as having the largest effect on marathon performance: *a*) $\dot{V}O_2$ at the ventilatory threshold, *b*) $\dot{V}O_{2max}$, and *c*) running economy. Athletes who have completed the "live high-train low" model of altitude training have demonstrated significant increases in $\dot{V}O_{2max}$ and $\dot{V}O_2$ at the ventilatory threshold (4), with no change in running economy (4, 5). Utilizing this data with the Joyner model predicts that a marathoner would experience an improvement of 4.7–5.1% over the 26.2 mile distance, dependent on having average or excellent running economy (1). We would offer that altitude training with the live high-train low model holds the largest (legal) ergogenic potential for the elite marathon athlete looking to break the 2-h barrier and would suggest that it be an integral part of any training plan toward that effort.

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A SMALL BODY MASS AND HIGHER MUSCLE RECRUITMENT STRATEGY IS THE KEY

TO THE EDITOR: The elegant Viewpoint by Joyner et al. (2) emphasizes that the best runners (East African) do not necessarily possess exceptional values for either $\dot{V}O_{2max}$ or lactate threshold. Therefore, the ability to run a fast marathon; at least in these individuals, likely is attributable to some other factor/s such as running economy, although its relationship with $\dot{V}O_{2max}$ is unclear (2). At least one other contributing factor could include attenuated heat accumulation, which, in long distance events is correlated with body mass (1). A higher body mass has been shown to reduce running speed particularly in hot conditions and there is evidence that marathon running is significantly hampered in ambient temperatures above 25°C (3, 5). It is also evident that reductions in running speed occur before significant elevations in core temperature and ahead of the expected heat accumulation to be achieved should a given running speed be maintained (4). Runners with smaller body mass can maintain higher speeds for less heat accumulation. Therefore, if a 2-h marathon is to be achieved it is likely that it will only be possible for individuals with a small body mass, generating and retaining less heat; however, to achieve this it will be necessary for that individual to sustain a higher skeletal muscle recruitment strategy over an extended period of the race.

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OPTIMIZING STRATEGIES FOR THE MARATHON

TO THE EDITOR: We are in overall agreement with the points that Joyner and coworkers (3) made in their Viewpoint paper. Maybe the main question that needs to be posed is as follows: Compared with the last decades, can the rate of improvement in the marathon world record improve in the next years? If this is true, the attainment of the 2-h barrier can occur earlier than Joyner et al. have predicted.

The question is obviously difficult to answer because marathon performance is likely multifactorial. Some of the main factors that determine world-class performance in this event are mostly of socioeconomic nature and difficult to control for in any prediction model. Indeed, increased prize money and competition opportunities allowing to earn a living running, largely explain the success of East African runners in the last decades (3).

On the other hand, a deeper understanding of the biological factors involved in marathon performance has arisen from recent research. Although world-class athletes are seldom used as subjects in scientific studies, this does not preclude that they cannot benefit from relevant findings obtained in less trained humans. Some aspects that could optimize the training efficacy of the best marathon runners include, among others, the following: *i*) use of heart rate variability (i.e., for training monitoring and overtraining prevention) (4); *ii*) respiratory muscle training (1); *iii*) optimal combination of hypoxic stimuli during daily living/training (5); and nutrition strategies (2).

We are not aware of any world-class marathoner who is combining all of the aforementioned advances to optimize his training regimens.

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TWO-HOUR MARATHON AND RUNNING ECONOMY

TO THE EDITOR: Joyner and colleagues (1) should be commended on tackling such a complex issue as to who and when will complete a 2-h marathon. Running economy is certainly an important factor in elite performance, despite this, it is relatively misunderstood. The authors indicate that an inverse relationship exists between mechanical efficiency and $\dot{V}O_{2max}$ in cyclists but has not been shown in runners. It has been demonstrated that $\dot{V}O_{2max}$ is inversely related to running economy (2) albeit in a small population of well trained runners. Indeed, others have suggested, if not outwardly proven that runners with good economy have lower $\dot{V}O_{2max}$ (3). Running economy relates to performance in distances from 800 m to 10 km not just the marathon, whereas $\dot{V}O_{2max}$ often does not show significant relationship to performance in elite runners (2).

The genetic influence on running performance may not be limited to a few select genes that happen to cosegregate with performance. The difference in running economy may be explained by lower leg volume as demonstrated in Kenyan runners (3). Joyner et al. (1) mention greater running economy found in Africans. Perhaps the anomaly runner that possesses both high $\dot{V}O_{2max}$ and greater running economy may be a result of as yet unanticipated gene pool mixing.

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OXIDATIVE STRESS: FRIEND AND FOE OF THE ELITE MARATHONER

TO THE EDITOR: Joyner et al. (5) nicely summarize major training and genotypic influences on the physiological capacity for world class marathon performance, yet make no mention of the central relationship between oxidative stress and these factors. Intermittent peaks of intracellular reactive oxygen and nitrogen species (RONS) generated during high-intensity exercise training initiate the cascade of events which ultimately lead to upregulation of intrinsic antioxidants and mitochondrial biogenesis to improve endurance performance (4). Paradoxically, oxidative stress is responsible for impaired muscle contraction during prolonged intense exercise and is therefore detrimental to race-day performance (6). Polymorphisms of intrinsic antioxidant genes are associated with racing-induced oxidative stress and muscle damage in runners (1), which further supports the potential contribution of genotype to the 2-h marathon.

Athletes often use antioxidant supplements in attempt to reduce the negative consequences oxidative stress. However, antioxidant supplementation may impair the normal hormetic response to prevent training adaptations to endurance exercise (3). Further research is necessary to determine the optimal timing and dosages of antioxidants to promote recovery rather than impair hormesis in world class athletes. Regardless, supplements that reduce oxygen consumption, and thus reduce oxidative stress, can prolong high-intensity exercise (2) and may help race-day performance.

We believe the first 2-h marathoner will achieve optimal performance through a fine balance between yet-undefined ideal genotypic factors. This athlete will combine training and nutritional practices that produce optimal fluctuations in oxidative stress for a maximal hormetic response during training and minimize RONS-associated impairments in performance on race day.

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CRITICAL VELOCITY AND MAXIMAL LACTATE STEADY STATE: BETTER DETERMINANTS OF 2-HOUR MARATHON

TO THE EDITOR: The achievement of a 2-h marathon depends on the running velocity associated with the highest obtainable level of steady state for one or more submaximal physiological variables. Joyner et al. (4) suggest that the lactate threshold (LT) is one such determinant variable, due in part to a strong correlation with marathon performance (4). However, the velocity at LT is lower than the average pace of a marathon (1), suggesting that the highest sustainable steady state is determined by other mechanisms. Maximal lactate steady state (MLSS) and critical velocity (CV) occur at similar velocities and metabolic rates (5) and define the highest intensity at which $\dot{V}O_2$ and fatigue-inducing metabolites such as blood and muscle H+ and Pi achieve steady-state values (3, 5). In addition, MLSS and CV occur at ~85–90% $\dot{V}O_{2max}$ (5), which is similar to the $\dot{V}O_2$ maintained by elite marathon runners when running for more than 1 h (4). Furthermore, CV is more highly correlated with marathon time than either $\dot{V}O_{2max}$ or ventilatory threshold (an estimate of LT) (2). Finally, MLSS and CV may be more trainable than either $\dot{V}O_{2max}$ or running economy. Therefore, we believe that to develop a successful strategy for training for a 2-h marathon, focus should be directed to a better understanding of the underlying mechanisms and trainability of MLSS and CV.

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THE TWO-HOUR MARATHON, WHO AND WHEN? HAÏLE GEBRSELASSIE IN 2000

TO THE EDITOR: As discussed by Joyner et al. (4), the physiological determinants of performance in long distance running include maximal aerobic power ($\dot{V}O_{2max}$) and lactate threshold. Additionally, the supremacy of East Africans among elite marathon runners is likely due to a superior running economy (5) originating from favorable physical features compared with Caucasian runners.

Most elite marathon runners usually begin competing in shorter distance races before moving onto longer distances in their later years. Although it is recognized that physical performances decline with age as $\dot{V}O_{2max}$ decreases, the last world records achieved in marathon was Haïle Gebrselassie at the age of 35.

In 2008, Gebrselassie won the Berlin Marathon with the world record time of 2:03:59. After the race, he told the French newspaper L'Equipe that he was too old to break the 2-h barrier (3). According to the formula by Daniels and Gilbert (2), a $\dot{V}O_{2max}$ of 86 ml·kg^{-1}·min^{-1} is required to break the 2-h barrier, whereas Gebrselassie's $\dot{V}O_{2max}$ was 82.8 ml·kg^{-1}·min^{-1} during the Berlin Marathon. Considering that ageing lowers $\dot{V}O_{2max}$ linearly [−0.43 ml/kg/min/yr (1)], we calculate that Gebrselassie had the necessary $\dot{V}O_{2max}$ when he was 27 yr old and could have run a marathon in 2 h in 2000.

Thus we predict that a world class marathon runner from East Africa, aged around 25 or less, could break the 2 h barrier if specifically trained early enough.

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THE TWO-HOUR MARATHON: GENETICS WILL BECOME INCREASINGLY IMPORTANT

TO THE EDITOR: In their Viewpoint, Joyner, Ruiz, and Lucia (2) correctly (in my view) give the topic of genetic predisposition for elite marathon performance some prominence. However, the total genotype score (TGS) data they cite, such as a TGS >75 providing a Caucasian individual with ~5 times greater chance of achieving elite endurance runner status, are preliminary at best—no doubt the authors realize this, but it is worth expanding on. The TGS approach we proposed (4) is entirely dependent on the appropriateness and completeness of the genetic variants included. So >75 is applicable to a specific phenotype in a specific population, for the 7 polymorphisms chosen in that specific study (3). If a future analysis includes additional polymorphisms for which there is evidence, e.g., only 1 of the 10 polymorphisms recently used (1) to characterize elite endurance athletes was also used by Ruiz et al. (3), then it is likely that a differently calculated TGS threshold will emerge that is more powerful in describing elite marathoners.

The progression of the marathon record over recent decades is a product of combined developments in year-round training, financial incentives, nutritional strategies, footwear, fast courses, favorable ambient conditions, etc. However, as these training, nutritional, and technological advancements become the norm, then over time, the spontaneous appearance of new, more favorable genetic combinations in individuals also born with the opportunity to train and compete will become steadily more important. The marathon record should continue to fall, but at a steadily reducing rate.

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THE TWO-HOUR MARATHON: PHYSIOLOGICAL AND BIOCHEMICAL FACTORS DETERMINANTS RUNNING ECONOMY

TO THE EDITOR: Running economy (RE) is one of factors that could be critical for performance in running endurance events such as marathon. Running efficiency is influenced by many factors such as environmental conditions, participant specificity and metabolic modifications. Marathon climate conditions vary not only according to the course geography but also can change from year to year and even from start to finish in the same race (1). The fact that climate can significantly limit temperature regulation and performance is evident from the correlation between the decreasing in RE during long-distance running and physiological factors such as the increasing of body temperature, a lack of fluid balance, and an increasing in circulating free fatty acids and glycerol (2). Moreover, a number of physiological and biochemical factors appear to influence RE in high trained athletes. These include metabolic adaptations within the muscle such as increased mitochondria and oxidative enzymes, the ability of the muscles to store and release energy (5), and physiological adaptations such as motor unit recruitment. Although a small improvement in RE could have a large impact on distance running performance, trained distance runners have shown an increasing in their RE following a period of resistance training (4). Consequently, as proposed by Joyner et al. (3), African athletes, who possess physiological advantages such as greater thermoregulation capacity, better RE, high skeletal oxidative capacity, higher skeletal enzyme activity, and superior resistance to fatigue, will be the first to run a sub-2-h marathon in a good psychological atmosphere and adequate diet.

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WHAT IS COEFFICIENT OF SPEED ENDURANCE TO ACHIEVE TWO-HOUR MARATHON?

TO THE EDITOR: The 2-h marathon has become a real possibility (3). We focused on speed endurance ability as key to running a marathon within 2 h. Speed endurance ability is defined here as the ratio of a marathon to the 10,000 m. The speed endurance coefficient of Haile Gebrselassie, the current men's marathon world record holder, is 4.70 (2:03:58/26:22, marathon/10,000 m). Interestingly, this coefficient endurance is not a surprising value. The coefficient endurance of the Japanese current top 10 marathon runners (4.52) is considerably higher than that of Gebrselassie. Most Japanese elite runners give priority to total running time over running speed. The large amount of running may induce a similar response to skeletal muscle in myocardial characteristics. Cardiac muscle cells contain a large number of mitochondria (~40% volume of cytoplasm), reflecting the high turnover rate in fat metabolism. In comparison to cardiac muscle, only ~5% of skeletal muscle fiber is occupied by mitochondria (1). Although marathon performance is influenced by various physiological and psychological factors (2), mitochondria function is noted as a possible limiting factor to aerobic capacity of human skeletal muscle (4). The large amount endurance training promotes a mitochondrial development (5), and this may contribute to enhancement of coefficient endurance. If Kenenisa Bekele, who is the current world record holder of 10,000 m (26:17), obtained the speed endurance coefficient achieved by Japanese elite runners (4.56), his marathon time would be 2 h!

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LOW PULMONARY VASCULAR RESISTANCE BREAKS THE TWO-HOUR MARATHON LIMIT

TO THE EDITOR: Joyner et al. (1) raise a thought-provoking question on the possibility of breaking the 2-h marathon barrier. They argue that a sub-2-h marathon is physiologically possible, and describe the systemic requirements of the ideal athlete. Yet, the importance of the pulmonary circulation in extreme physical circumstances such as the marathon should not be overlooked. Interestingly, the structure of the pulmonary vasculature does not change in response to training, but a large lung-to-body weight ratio is associated with a large exercise-capacity (3). During heavy exercise, pressure in the pulmonary circulation, and thereby right ventricular afterload, may increase by as much as 70% (5) and likely remains elevated throughout a marathon. In some race horses, this increase in pulmonary pressure even results in capillary bleeding and pulmonary edema and limits exercise-capacity (5). Pulmonary vasodilators serve to limit the increase in pulmonary artery pressure and in right ventricular afterload. Indeed, in patients with pulmonary hypertension, pulmonary vasodilators significantly improve exercise capacity (5). High plasma levels of NO and low plasma levels of endothelin-1 have been detected in trained individuals (4) and promote pulmonary vasodilation and limit the increase in pulmonary pressure during exercise (2). Thus marathon runners with high NO levels and low endothelin-1 levels in addition to a large lung-to-body weight ratio are most likely to be excellent performers, because their pulmonary vascular resistance and right ventricular afterload are low. The pulmonary vascular structure and regulation of its function in elite marathon runners deserve further investigation, as it is reasonable to believe that those with the lowest pulmonary vascular resistance during the marathon may ultimately finish it within 2 h.

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GENETIC INFORMATION WILL INFLUENCE BUT NOT PREDICT THE FIRST TWO-HOUR MARATHON

TO THE EDITOR: We strongly agree with Joyner et al. (1) that genotype/phenotype associations in general and associations with endurance performance in particular should be thought of as probabilistic rather than deterministic. For example, power athletes can achieve elite levels despite having the “wrong” ACTN3 genotype (2), and a large percentage of the Spanish population carries the genotype combination predicting elite marathon performance, yet few actually reach that level (3). Aggregate genotype scores such as the TGS (5) are superior to the measurement of single gene variants, but they operate under the assumption that the most important variants have been included in the model. Unfortunately, performance is a remarkably complex trait influenced by hundreds of genes, the vast majority of which are currently unknown. Sophisticated studies have explained only a fraction of the genetic contribution to gains in $\dot{V}O_{2max}$, which is but one contributor to performance (4). We are left with physical and environmental characteristics (e.g., geographic ancestry, training history, physiological measures) that predict performance far better than any current or anticipated genotype profile. Gathering additional information on genotype is unlikely to enable such performance predictions given both the limitations of our knowledge of contributing gene variants and the complexity of the performance phenotype. Instead, genetic factors, in unique combination with training history, physiological traits, environmental conditions, and other intangibles will come together to produce the first sub-2-h marathon and any contributing gene variants are likely to be as unique as the assemblage of other factors that lead to the feat.

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TWO-HOUR MARATHON REQUIRES MOTHER NATURE’S HELP

TO THE EDITOR: Joyner et al. (4) are to be congratulated for their insightful analysis of prospects for a 2:00:00 marathon, a challenge comparable to the 4:00 mile 100 yr ago. Achieving this will require longer than evident in their analysis. The shape of the record progression curve is a negatively accelerated polynomial predicting 2:00:00 in ~2099.

Further adaptations of $\dot{V}O_{2max}$ or running economy are unlikely without doping, changes in shoe technology, or child production among elite runners, allowing for uniquely favorable genetic combinations. The %$\dot{V}O_{2max}$ sustainable for 2 h is likely limited by the rate increase in core temperature (Tc)(5). To increase running velocity by ~10 m/min to gain the required 4 min requires an increase in $\dot{V}O_2$ from ~64.0 to 66.5, or ~2.5 $ml \cdot min^{-1} \cdot kg^{-1}$; ~48 W metabolic power). Heat balance modeling by Daanen et al. (1) suggests increased running speed increases convective heat loss (~10 W). Assuming sweat rates of 800 ml/h, the current WR performed at 12°C (Berlin WR began at 10°C, increased to 14°C), results in a final Tc of 40°C. At 12°C Tamb, for 2:00:00, the final Tc would be an unacceptable 42°C. Assuming no other changes in heat removal capabilities, the only scenario allowing increased metabolic rate without critical hyperthermia, known to slow marathon performance (2, 3), is via increases in environmental heat loss, requiring a decrease in Tamb to <11°C.

Thus achieving 2:00:00 may be possible by current runners if uniquely cool conditions are encountered, which may depend on the cooperation of Mother Nature.

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THE HIGHEST POSSIBLE SKELETAL MUSCLE METABOLIC STABILITY AS A KEY FACTOR FOR BREAKING THE 2-HOUR MARATHON BARRIER

TO THE EDITOR: We agree with Joyner et al. (2) that outstanding running economy is one of the necessary factors required to break the 2-h marathon barrier. It should be noted, however, that running economy can be affected by a disturbances in muscle metabolic stability, expressed by decreases in muscle [PCr] and DGATP as well as by increases in π, [ADPfree], [IMPfree], [AMPfree], and [H+] (4). There is indeed convincing evidence that muscle fatigue can decrease muscle efficiency due to muscle metabolites accumulation (3). The concept at the base of the "slow component" of O_2 kinetics is that fatiguing muscles consume progressively more O_2 per unit of time to maintain a given work rate. Or, conversely, that fatiguing muscles reduce force or power output to avoid the slow component (4). Interestingly, it was demonstrated that high-class marathon runners perform their marathon race at the highest possible running velocity at which they can maintain unchanged blood pH (5) and presumably the highest running economy throughout the race. To break the 2-h marathon barrier the elite runners will have to improve their muscle metabolic stability to maintain the highest possible running economy while performing the marathon race at the speed exceeding 21 km/h. The locomotor muscles of these runners should possess an excellent muscle metabolic stability—as close as possible to that found in the heart, the most fatigue-resistant muscle (1). Runners with very high muscle metabolic stability could break the 2-h marathon barrier.

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THE TWO-HOUR MARATHON: THE IMPORTANCE OF BREATHING ECONOMY

TO THE EDITOR: A number of important questions remain regarding if and when the 2-h marathon threshold will be crossed. Although we can't say for certain when this achievement will be accomplished, the pulmonary system, particularly through the impact of lung mechanics and respiratory metabolic properties on blood flow distribution, may be key and an underappreciated determinant of performance (3). As endurance athletes push the limits on running economy and the percentage of sustainable $\dot{V}O_{2peak}$, respiratory muscle work can rise abruptly as lung mechanical limits are approached, particularly expiratory flows near end-expiratory lung volume. This marked rise in ventilatory work equates to a large rise in the O_2 cost of the respiratory muscles, which can be as high as 15% of cardiac output (1, 3). There also can be large differences in lung volumes and flow rates across sexes and racial groups that could alter respiratory muscle O_2 cost. Studies have suggested that diaphragm and accessory muscle fatigue becomes evident when approaching workloads of 85–90% of peak (2). This fatigue has been demonstrated to cause a prioritization of blood flow delivery to the respiratory muscles as a result of respiratory muscle metaboreflex initiated vasoconstriction in the locomotor muscles (4). With this, the locomotor muscle vasoconstriction may contribute to activation of the locomotor metaboreflex, which in turn augments neural ventilatory drive and ultimately closes the negative feedback loop. Thus, perhaps in the end, it comes down to the economy of breathing rather than the more commonly debated economy of running.

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THE TWO-HOUR MARATHON: HOW?

TO THE EDITOR: Running economy (RE) and genetic factors have been suggested to be very important (3), although no evidence has been reported on the relationship between them. Interestingly, the recent literature have showed a relationship between lower limb's passive stiffness and RE (2) and between running performance and the COL5A1 gene (4), which is a gene that has been also related to flexibility (1). Thus it may be suggested that this gene could be potentially important for an exceptional RE. Another interesting hypothesis refers to epigenetics. It may be suggested that RE improvements could be related to the genetic expression of connective tissue adaptations. Moreover, as some forms of strength training have been demonstrated to be related to RE improvements (5), it is plausible that lower limb's elasticity may be altered with some training modalities favoring the elastic energy recoil.

Also, it should not be forgotten other cultural and psychological factors that are unavoidable. In fact, the extraordinary record improvements since Africans entered international competition (3) may be an evidence of the influence of such factors. Furthermore, another question arises regarding epigenetics and the influence of the "non-hereditary environmental influences" (3) that could interact with genetics. From a mechanistic point of view, it may be considered the role of the genotype and the genetic expression of the factors involved during adaptations to training. From a holistic point of view, we suggest the study of the interaction of the "non-hereditary environmental influences" with genetic factors that could be a more appropriate model.

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THE ATHLETE WITH MAINTAINED CEREBRAL OXYGENATION BREAKS THE RECORD

TO THE EDITOR: Only an athlete with favorable genes, a small body size, and an outstanding running economy will break the 2-h marathon barrier (2). It is equally important how he plans the run. Physiological and neurological stimuli need to be integrated in the brain and seen in that perspective; cerebral oxygen and substrate homeostasis may become affected by the marked increase in pulmonary ventilation during intense running that lowers the arterial CO_2 tension. Hyperventilation restrains cerebral blood flow and in turn cerebral oxygenation as demonstrated both by near-infrared spectroscopy (NIRS) and calculation of changes in the cerebral mitochondrial O_2 tension (4). A decrease in cerebral oxygenation seems important for development of fatigue as illustrated when the increase in cardiac output and cerebral perfusion are attenuated by β_1-adrenergic receptor blockade that not only lowers work capacity but also cerebral oxygenation (5). Importantly, with and without β_1-blockade, exercise is terminated at a similar reduction in cerebral oxygenation (5). Conversely, when cerebral oxygenation is restored by inhalation of an oxygen-enriched atmosphere, exercise capacity is enhanced (3). In long-distance running athletes appear to maintain their pace at a level that does not threaten cerebral oxygenation, and only when subjects raise the speed toward the end of the race cerebral oxygenation becomes low (1). Thus beside being provided with the best possible genotype, a perfect body size, and outstanding running economy, the athlete who breaks the 2-h marathon barrier needs to maintain a pulmonary ventilation that does not affect the arterial CO_2 tension and, in turn, cerebral blood flow and oxygenation. We suggest that such an athlete demonstrates a low ventilatory drive.

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DO NOT UNDERPLAY THE ROLES OF $\dot{V}O_{2max}$ AND CENTRAL FATIGUE IN THE 2-H MARATHON

TO THE EDITOR: Running velocity at $\dot{V}O_{2max}$ and lactate threshold and running economy (RE) independently accounted for 90 to 97% (R2) of 16-km run time (3). However, stepwise analysis attributed running performance mainly to $\dot{V}O_{2max}$ (90.2%), minimally to RE (7.1%), and not to lactate threshold; 97.3% $\dot{V}O_{2max}$ and RE combined (3). These data suggest that RE contributes to running performance in an additive manner at a given percentage of $\dot{V}O_2$ (4), and that RE translates to superior running performance in combination a high $\dot{V}O_{2max}$ and not independently. The data also disagree with the suggestion that exceptional RE may play more important roles than $\dot{V}O_{2max}$ in breaking the 2-h marathon performance barrier (1).

The central fatigue mechanisms may also limit the potential for further improvements in running performance in humans.

Although the exact pathways of the central fatigue mechanism are unclear presently, there is consensus that stress-related signals relayed from the various physiological systems to the brain during intense exercise can trigger efferent signals to induce fatigue and limit performance (2). The ability to achieve the 2-h marathon performance may ultimately depend on the potential and limitations of the human body design, which may be regulated through the central fatigue mechanisms. From a genetic point of view, the chance of having one individual in the world endowed with the perfect genetic make-up for superior endurance performance is only 0.0005% (5), that is, provided he/she likes to run.

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