Ultramarathon Running: Medical Issues

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13.1 Ultramarathons

13.1.1 What Is an Ultramarathon?

An ultramarathon is defined as any sporting event involving running longer than the traditional marathon length of 42.195 km [1]. Therefore, the shortest ultramarathon is the 50-km ultramarathon. Ultramarathons can be held as distancelimited races in kilometers or miles and in time-limited races in hours or days [1].

13.1.2 Who Are Ultramarathoners?

 In recent years, Hoffman systematically investigated sociodemographic characteristics of ultramarathoners $[2, 3]$. In a survey completed by 489 of 674 runners competing in two of the largest 161-km ultramarathons in North America, respondents had a mean age of 44.5 years and were generally men (80.2 %), were married (70.1 %), and had bachelor's (43.6%) or graduate (37.2%) degrees $[2]$. In the Ultrarunners Longitudinal Tracking (ULTRA) Study, Hoffman

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and Krishnan $\begin{bmatrix} 3 \end{bmatrix}$ interviewed a total of 1345 current and former ultramarathoners. Median age at the first ultramarathon was 36 years, and the median number of years of regular running before the first ultramarathon was seven $[3]$. The age at the first ultramarathon did not change across the past several decades, but there was evidence of an inverse relationship between the number of years of regular running before the first ultramarathon and the calendar year $[3]$. The active ultramarathoners had a previous year median running distance of 3347 km, which was minimally related to age but mostly related to their longest ultramarathon competition of the year $[3]$.

13.1.3 Women in Ultramarathons

 The share of women competing in ultramarathons was very low in the beginning of ultramarathon running. In 161-km ultramarathons held in the USA, the participation among women increased from virtually none in the late 1970s to nearly 20 % since 2004 $[4]$. Their percentage is now at ~20 % $[4-6]$. In two of the toughest ultramarathons in the world, women accounted on average for ~21.5 % in "Badwater Ultramarathon" and \sim 10.8 % in "Spartathlon" [5]. In most ultramarathons, the number of female finishers increased across years $[5, 6]$ $[5, 6]$ $[5, 6]$. For example, in the "Swiss" Alpine Marathon" in Switzerland, women's participation increased from \sim 10 % in 1998 to \sim 16 % in 2011 [6]. In "Badwater Ultramarathon" and

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"Spartathlon," there was an increase in female participation in "Badwater Ultramarathon" from 18.4 to 19.1 % and in "Spartathlon" from 11.9 to 12.5 $\%$ [5]. The rather low female participation might have different reasons. A potential explanation might be motivation. Female ultramarathoners were task- oriented, internally motivated, health, and financially conscious individuals [7]. Men, however, trend rather to compete in order to beat a concurrent or to win a race.

13.1.4 Where Are Ultramarathons Held?

 Ultramarathon races are offered all over the world. There are some of the most famous races such as the "Badwater Ultramarathon" (held in USA), the "Spartathlon" (held in Greece), and the "Marathon des Sables" (held in Morocco) just to name the best known $[1]$. Some of these races are held under extreme conditions such as extreme heat [8]. A problem of races held in heat is the fact that performance will be impaired $[9, 10]$ $[9, 10]$ $[9, 10]$. A very recent study showed that athletes would benefit from heat acclimation. Exposure to at least 2 h of exercise-heat stress on at least two occasions in the days may help in preventing exertional heat illnesses and optimizing performance outcomes in ultra-endurance runners in multistage ultramarathon competition in the heat $[11]$.

13.1.5 Where Do Ultramarathoners Originate From?

 It is well known that East-African athletes such as Kenyans and Ethiopians dominate the marathon events all over the world for decades [12, 13]. In ultramarathon running, however, athletes from other regions were dominating both participation and performance. For example, in 100-km ultramarathons, most of the finishers originated from Europe, in particular from France [14]. The number of finishers from Japan, Germany, Italy, Poland, and the United States of America increased exponentially between 1998 and 2011. For women, runners from Canada became slower while those from

Italy became faster. For men, runners from Belgium, Canada, and Japan became slower. Between 1998 and 2011, the ten best race times were achieved by Japanese runners for both women with \sim 457 min and men with \sim 393 min [14]. In ultramarathons longer than the 100 km, athletes from other countries seemed to dominate participation and performance. Ultramarathoners competing in the world's most famous races "Badwater Ultramarathon" (USA) and "Spartathlon" (Greece) originated from different regions [\[15 \]](#page-8-0). In "Badwater Ultramarathon," most of the finishes were achieved by athletes originating from the USA, followed by athletes from Germany and Great Britain. In "Spartathlon," however, the highest number of finishes was obtained by athletes from Japan, followed by athletes from Germany and France. Regarding performance, however, athletes from other countries were dominating. In "Badwater Ultramarathon," women from the USA were the fastest, followed by women from Canada. For men, the fastest finishes were achieved by competitors from the USA, followed by athletes from Mexico and Canada. In "Spartathlon," the fastest female finishes were obtained by women from Japan, followed by women from Germany and the USA. In men, the fastest finishes were achieved by runners from Greece, followed by athletes from Japan and Germany [15]. In the "Marathon des Sables" held in the Moroccan desert, local athletes seemed to dominate $[8]$. In men, Moroccans won nine of ten competitions, and one edition was won by a Jordanian athlete. In women, however, eight races were won by Europeans (i.e., France five, Luxembourg two, and Spain one, respectively), and two events were won by Moroccan runners $[8]$.

13.2 Are Ultramarathoners Different to Marathoners?

 Several studies compared recreational marathoners to recreational ultramarathoners regarding anthropometric $[16, 17]$ $[16, 17]$ $[16, 17]$ and training $[16-19]$ characteristics. Most probably, ultra-runners start with a marathon before completing the first ultramarathon. In ultramarathoners, the number of previously completed marathons is significantly

higher than the number of completed marathons in marathoners. However, recreational marathoners have a faster personal best marathon time than ultramarathoners. Successful ultramarathoners have \sim 8 years of experience in ultra-running. Ultramarathoners complete more running kilometers in training than marathoners do, but they run more slowly during training than marathoners [18, 19].

 Marathoners show difference in anthropometry compared to ultramarathoners. When marathoners were compared to 100-km ultramarathoners $[16]$, marathoners had a significantly lower calf circumference and a significantly thicker skinfold at pectoral, axillary, and suprailiacal sites compared to ultramarathoners. When marathoners were compared to 24-h ultramarathoners $[17]$, ultramarathoners were older, had a lower circumference at both the upper arm and thigh, and a lower skinfold thickness at the pectoral, axillary, and suprailiacal sites compared to the marathoners.

 Marathoners show also differences in training compared to ultramarathoners. Marathoners rather rely on a high running speed during training $[16]$, whereas ultramarathoners rely on a high running volume during training $[16, 19]$. When marathoners were compared to 100-km ultramarathoners [16], marathoners completed fewer hours and fewer kilometers during the week, but they were running faster during training than ultramarathoners. When marathoners were compared to 24-h ultramarathoners, the ultramarathoners were running for more hours per week and completed more kilometers during training, but were running slower than the marathoners $[17]$. An interesting recent finding was that ultramarathoners have a greater pain tolerance than controls $[20]$. This fact might enable ultra-runners to endurance longer under different circumstances than others.

13.3 Predictor Variables for Successful Ultramarathon Running

In recent years, several studies tried to find the most important predictor variables for a successful outcome in ultramarathon running. Among

these variables, the most important were age $[16, 21]$, anthropometric characteristics such as body fat $[16, 19]$, body mass index $[22]$ and limb circumferences [23], training characteristics such as running speed $[16, 19, 21]$ and training volume $[16, 19, 21]$ $[16, 19, 21]$ $[16, 19, 21]$ $[16, 19, 21]$ $[16, 19, 21]$, and previous experience $[24, 25]$ $[24, 25]$ $[24, 25]$.

 Regarding anthropometric characteristics, leg skinfold thickness – which was highly predictive of short-distance runners $[26]$ – was only predictive in bivariate analyses, but not in multivariate analyses, with ultramarathon running performance $[24, 27]$ $[24, 27]$ $[24, 27]$. In ultramarathoners, body mass index and body fat seemed to be more important anthropometric characteristics $[22, 28]$ $[22, 28]$ $[22, 28]$. In 161km ultramarathoners, lower values of body mass index were associated with faster race times [22]. Body fat is also an important anthropometric predictor variable. In 161-km ultramarathon running, faster men have lower percent body fat values than slower men, and finishers have lower percent body fat than non-finishers $[28]$.

 When different characteristics such as skeletal muscle mass, body fat and training characteristics were investigated in multivariate analyses, and body fat and training characteristics were associated with running times in ultramarathoners [19]. For 100-km ultramarathoners, weekly running kilometers and average speed during training were negatively related to race time and the sum of skinfolds was positively related to race time $[25]$. Apart from anthropometric and training characteristics, age seems also to be an important predictor variable for ultramarathon performance. In 100-km ultramarathoners, age, body mass, and percent body fat were positively related to race times and weekly running kilometers were negatively related to race times [16].

 Previous experience seems, however, to be the most important predictor variable in ultramarathon performance $[22, 24, 29]$ $[22, 24, 29]$ $[22, 24, 29]$. For example, personal best marathon time was a predictor variable in mountain ultramarathoners [22]. In 24-h ultramarathoners, anthropometry and training volume seemed not to have a major effect on race performance [24]. However, a fast personal best marathon time seemed to have the only positive association with race performance $[24]$. To achieve a maximum of kilometers in a 24-h

 ultramarathon, ultra-runners should have a personal best marathon time of ∼3 h 20 min and complete a long training run of ∼60 km before the race, whereas anthropometric characteristics such as low body fat or low skinfold thicknesses showed no association with performance [29].

13.3.1 Performance in Women and Men and Sex Difference in Performance

 Generally, women compete slower than men in ultramarathon running $[6, 30, 31]$ $[6, 30, 31]$ $[6, 30, 31]$ $[6, 30, 31]$ $[6, 30, 31]$. Coast et al. [31] compared the world best running performances for race distances from 100 m to 200 km. The running speeds were different between women and men with the average difference being 12.4 $%$ faster for men. There was a significant slope to the speed difference across distances where longer distances were associated with greater differences $[31]$. In 24-h ultramarathons held between 1977 and 2012, the sex differences were \sim 5 % for all women and men, \sim 13 % for the annual fastest finishers, \sim 13 % for the top ten, and \sim 12 % for the top 100 finishers [30].

 However, women were able to reduce the sex gap in recent years $[6, 30, 32]$. For example, in 24-h ultramarathons, the sex differences decreased for the annual fastest to \sim 17 %, for the annual ten fastest to \sim 11 %, and for the annual 100 fastest to \sim 14 % [30]. Across years, female and male ultramarathoners improved performance $[6, 32]$. In 100-mile ultramarathons, the fastest women and men improved their race time by $∼14$ % across the 1998–2011 period [32].

13.3.2 The Age of Peak Ultramarathon Performance

 The age of peak ultramarathon performance and a potential change in the age of peak performance have been intensively investigated in very recent years $[5, 6, 30, 32-36]$ $[5, 6, 30, 32-36]$ $[5, 6, 30, 32-36]$. Generally, the best ultramarathon performance is achieved at higher ages than the best marathon performance. The fastest marathoners achieved their best times at the age of ~29.8 years for women and ~28.9 years for men [37]. In 100-km ultramarathon running, the best race times were observed between 30 and 49 years for men and between 30 and 54 years for women $[34]$. In 161-km ultramarathoners, the fastest times were achieved by athletes ranked in the 30–39-year age group for men and the 40–49 year age group for women [38].

 Generally, women achieved the best ultramarathon performance at about the same age like men [30, 32]. For 100-km ultramarathoners, the age of the fastest female and male finishers remained unchanged at ∼35 years between 1960 and 2012 [33]. In 24-h ultramarathoners, the best performances were achieved at $~40-42$ years [35].

In some instances, the age of the fastest finishers increased across years $[6]$; in other instances, it remained unchanged $[30, 32]$ or it even decreased $[5]$. For example, in the annual fastest male 24-h ultramarathoners, the age of peak running speed increased from 23 years (1977) to 53 years (2012) [30]. There seemed to be a trend that the fastest finishers were older in the very long ultramarathon distances $[30, 32]$. In 100mile ultramarathoners, the mean ages of the annual top ten fastest runners were ~39 years for women and \sim 37 years for men [32]. In 24-h ultramarathoners, the ages of peak running speed were unchanged at ~41 and ~44 years for the annual ten and the annual 100 fastest men, respectively. For women, the ages of the annual fastest, the annual ten fastest, and the annual 100 fastest remained unchanged at \sim 43 years, respectively [30]. In "Badwater Ultramarathon" and "Spartathlon" as two of the toughest ultramarathons in the world, the fastest race times were achieved by athletes at the age of $~10-42$ years [36].

 Generally, the number of master ultramarathoners increased and their performance improved in recent years [39, [40](#page-9-0)]. For example, in the "Swiss Alpine Marathon," the number of women older than 30 years and men older than 40 years increased and performance improved in women aged $40-44$ years $[40]$. In the "Marathon" des Sables," the number of finishers of master runners older than 40 years increased for both sexes and men aged 35–44 years improved running speed $[39]$. A potential explanation for the

rather high age of ultramarathoners could be the finding that the median age at the first ultramarathon was 36 years in the study of Hoffman and Krishnan $\begin{bmatrix} 3 \end{bmatrix}$ when investigating 1345 current and former ultramarathoners.

13.4 Physiology of Ultramarathon Running

13.4.1 Energetic Demands During Ultramarathon Running

 Successful completion of an ultramarathon such as the 161-km "Western States Endurance Run" is related to large consumption rates of fuel, fluid, and sodium $[41]$. During ultramarathon running, the most important energy source is carbohydrates $[42-44]$. In 100-km ultramarathoners, 88.6 % derived from carbohydrate, 6.7 % from fat, and 4.7 $%$ from protein [44]. In one ultramarathoner completing a 1005-km race over 9 days, the nutrient analysis showed an average daily energy intake of 25,000 kJ with 62 % from carbohydrate, 27 % from fat, and 11 % from protein. Carbohydrate intake was estimated to be 16.8 g/ kg/day and protein intake was estimated to be 2.9 $g/kg/day [43]$.

 Generally, ultramarathoners are not able to meet their energetic demands during a race $[45,$ [46](#page-9-0)], and a partially considerable energy deficit results [45, 47, 48]. The insufficient energy intake in ultra-endurance athletes is also associated with a low antioxidant vitamin intake $[46]$. The large energy deficit is caused by inadequate energy intake, possibly due to suppressed appetite and gastrointestinal problems [45]. Ultramarathoners often suffer from problems with digestion [49] and gastrointestinal bleeding after an ultramarathon is not uncommon $[50]$. It has been shown that lower gastrointestinal symptoms correlate with gastrointestinal bleeding $[50]$. In a mountain ultramarathon, 43 percent of all subjects complained of gastrointestinal distress during the race $[49]$. A potential reason for these problems could be that exercise has been found to alter esophageal motility [51]. However, also prerace experience could be an explanation. Runners with gastrointestinal distress tended to complete fewer training miles and to do shorter training runs $[52]$. The result of the energy deficit is a decrease in body mass where both lean body mass (skeletal muscle mass) and fat mass will be reduced [53, [54](#page-9-0)].

13.4.2 Fluid and Electrolyte Metabolism During Ultra-Running

 Ultramarathoners need to consume large amounts of fluids to prevent dehydration during running. During ultramarathon running, the largest decreases in body mass occur in the first hours of the race $[55]$. Large fluid intakes might, however, lead to an increased risk for exerciseassociated hyponatremia, defined as plasma sodium concentration $[Na^+]$ <135 mmol/l. Several cases of hyponatremia, with symptoms including altered mentation, seizures, and pulmonary edema, have been reported in endurance athletes over the last few years. This condition has been observed most frequently in individuals participating in ultra- distance events but has also been reported in marathon runners. Excessive water intake has been identified as a common etiological factor [56].

 However, there seemed to be no need to consume excessive amounts of fluid in ultramarathon running [57]. Generally, ultramarathoners seemed not to overdrink $[58]$ and no fluid overload should occur during an ultramarathon [59]. In a 100-km ultramarathon, faster runners drank more fluid than slower runners and faster runners lost more body mass than slower runners. Additionally, runners lost more body mass when they drank less fluid $[57]$. Faster running speeds were associated with larger body mass losses. Therefore, athletes who drink less during ultramarathon running may profit from body mass loss and complete the race faster [57]. Also in a 160-km ultramarathon, greater loss in body mass during the race was not associated with impaired performance but was rather an aspect of superior performance $[60]$.

13.5 Medical Disturbances Related to Ultramarathons

13.5.1 Exercise-Associated Hyponatremia in Ultramarathon Running

 Exercise-associated hyponatremia is a rather frequently found electrolyte disorder in ultramarathoners $[11, 61-63]$ $[11, 61-63]$ $[11, 61-63]$ where high ambient temperatures might be of high importance $[11]$, 64. In a five-stage 225-km multistage ultramarathon where athletes competed at temperatures of up to 40 °C, the prevalence of exercise-associated hyponatremia amounted to 42 $\%$ [11]. In the 2008 "Rio Del Lago 100-Mile Endurance Run" in Granite Bay, California, the prevalence of exercise-associated hyponatremia was at 51.2 $%$ [64].

 Exercise-associated hyponatremia is relatively uncommon in temperate climates $[65-69]$. In a seven-stage 350-km multistage mountain ultramarathon at moderate to low temperatures, the prevalence of exercise-associated hyponatremia was at 8 % $[66]$. In a 100-km ultramarathon $[67]$, 68] and a 24-h run $[69]$ held at moderate to low temperatures, no cases of exercise-associated hyponatremia were recorded.

 The country where the ultramarathon is held seemed to be of importance. In races held in the USA, the prevalence of exercise-associated hyponatremia was higher than in races held in Europe. In the 2009 edition of the "Western States Endurance Run," the prevalence of EAH was 30 $\%$ [61]. In ultramarathons held in Switzerland, Europe, the prevalence of exerciseassociated hyponatremia was between 0 and 8 % $[66, 67, 69]$ $[66, 67, 69]$ $[66, 67, 69]$ $[66, 67, 69]$ $[66, 67, 69]$. Also in ultramarathoners competing in the Czech Republic, Europe, the prevalence of exercise-associated hyponatremia was low [70].

An increased fluid intake during ultramarathon running might also have negative effects on the feet since recent studies showed an association between fluid intake and limb swellings $[71, 72]$. Fluid intake was related to the changes in limb volumes, where athletes with an increased fluid intake developed an increase in limb volumes [71]. An increase in feet volume after a 100-km ultramarathon was due to an increased fluid intake $[72]$.

13.5.2 Pathophysiological Effects of Ultramarathon Running

 Running an ultramarathon may lead to other disturbances apart from exercise-associated hyponatremia. Ultramarathon running is associated with a wide range of significant changes in hematological parameters, several of which are injury related. A single bout of strenuous running exercise results in perturbations to numerous biomarkers, and the magnitude of changes to biomarkers is proportional to the severity of the running bout [73]. Ultramarathon running can produce changes to biomarkers that are normally associated with pathology of the muscles, liver, and heart [74–76]. However, also markers of the inflammatory response such as C-reactive protein [77–79] and IL-6 [77, 79, [80](#page-10-0)] become elevated. Examples for biomarkers of pathology of muscles, liver, and heart are cardiac troponins, plasma volume, myoglobin, leucocytes, sodium, chloride, urea, alkaline phosphatase, gamma- glutamyl transferase, alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, creatine kinase, bilirubin, total protein, albumin, glucose, calcium, and phosphate $[73-76, 80-82]$. A number of variables remain within normal limits despite severe physical stress $[80]$. These changes are transient, and full recovery generally occurs within days and without any apparent long-term adverse consequences $[73, 76]$. For example, a 48-h ultramarathon caused hypocapnic alkalosis with slight hyperkalemia and hypocalcemia, but no hyponatremia. Blood biochemistry showed severe muscle but not liver damage and an acute inflammatory response [83]. Most of the changes were dissolved after 48 h of recovery $[83]$.

 Prolonged running is also known to induce hemolysis. It has been suggested that hemolysis may lead to a significant loss of red blood cells [84]. However, in a 166-km mountain ultraendurance marathon, "exercise anemia" was entirely due to plasma volume expansion and not to a concomitant decrease in total red blood cell volume $[84]$.

 Apart from these biomarkers, also changes in hormones have been documented [85, 86]. After a 110-km ultramarathon, cortisol was increased and

testosterone decreased [85]. In the 1000 km Sydney to Melbourne ultramarathon, resting serum conjugated catecholamines such as epinephrine, norepinephrine, dopamine, free epinephrine, and free dopamine were significantly elevated above the normal mean [86]. Adrenocorticotropic hormone (ACTH) levels were significantly elevated above the normal range. Immunoreactive beta-endorphin, growth hormone, prolactin, testosterone, cortisol, and cortisol-binding globulin were within the normal range. After the race, catecholamines, free and conjugated, remained significantly elevated above the normal mean. ACTH remained elevated and immunoreactive beta-endorphin within the normal range. A significant increase in growth hormone, prolactin, and cortisol was seen, with no change in cortisol-binding globulin. The authors concluded that these ultramarathoners demonstrated a significantly altered baseline hormonal state as a model of chronic physical stress $[86]$. This may represent hormonal adaptation to prolonged stress.

13.5.3 Ultra-running and Skeletal Muscle Damage

 Ultramarathon running has a major impact on skeletal muscles [74]. Unfamiliar exercise involving forceful eccentric muscle contractions, such as running downhill, can cause increases in creatine kinase (CK) and delayed onset of muscle soreness that peaks \sim 36–72 h after the exercise bout [73]. In ultramarathoners, a partially considerable increase in CK can be found postrace $[63, 74, 78, 87]$. For example, CK was increased 35-fold at the end of a 200-km race and remained increased until day 5 [78]. In another 200-km ultramarathon, CK increased 90-fold postrace [74]. In "Badwater Ultramarathon," CK can increase up to 27,951 U/l [87]. And in the 161-km "Western States" Endurance Run," 216 (66 $\%$) of 328 finishers had median and mean CK concentrations of 20,850 U/l and 32,956 U/l, respectively, with a range of 1500–264,300 U/l, and 13 (6 %) of the finishers had values greater than $100,000$ U/l $[88]$.

 The increase in CK seemed to be dependent upon the fitness level of the athlete $[63]$. Higher levels of training, or previous ultramarathon

 racing experience, or both, were associated with lower immediate postexercise levels of plasma enzyme activity $[63]$.

 Several studies showed that ultramarathon running leads to a substantial decrease in skeletal muscle mass $[57, 89, 90]$. It has been tried to prevent the decrease in skeletal muscle mass by the intake of amino acids [89]. However, BCAA supplementation before and during a 100-km ultramarathon had no effect on performance, skeletal muscle damage $[89]$, and muscle soreness $[90]$.

13.5.4 Ultra-running and Heart Damage

 Several studies investigated a potential damage of ultra-running to the heart since cardiac muscle injury markers such as CK, creatine kinasemyocardial band (CK-MB), cardiac troponin I (cTnI), and cardiac muscle strain marker, N-terminal pro-brain natriuretic peptide (NT-proBNP), were elevated postrace $[87, 91, 91]$ $[87, 91, 91]$ $[87, 91, 91]$ 92]. Also highly sensitive troponin I was released during ultramarathon running [93, [94](#page-11-0)].

The findings whether a damage of the heart muscle occurs or not are controversial. Highintensity endurance exercise is associated with biochemical abnormalities that may reflect adverse consequences on cardiac structure and biology $[94]$. In 18 male marathoners with average age of ~53 years competing in a 308-km ultramarathon, a normal CK-MB mass index (<5.0 ng/ml) and the absence of an increase in the cTnI levels after the ultramarathon suggested that no myocardial injury despite an elevation in $CK-MB$ occurred $[91]$. Also in ultramarathoners competing in "Badwater Ultramarathon ," strenuous endurance exercise under extreme environmental conditions did not result in structural myocardial damage in well-trained ultra-endurance athletes $[87]$. Matin et al. $[95]$ showed in 77 % of ultramarathoners an elevated activity of serum CK-MB, but cardiac scintigraphy showed no evidence of myocardial injury.

 On the other side, in a study investigating competitors in the two-day "Lowe Alpine Mountain Marathon," echocardiographic results indicated left ventricular diastolic and systolic dysfunction following cessation of exercise [96]. Humoral markers of cardiac damage were elevated and the elevations of cardiac troponin were suggestive of minimal myocardial damage [96]. After a 24-h ultramarathon, two of 20 runners showed a slight increase in troponin levels. One of them also had simultaneous decrease in left ventricular ejection fraction. Basal echocardiography assessment showed left ventricular hypertrophy in one and increased left atrial volume in five runners [97]. Estorch et al. $[98]$ showed in runners that myocardial MIBG (123I-metaiodobenzylguanidine) activity was decreased after a 4-h run. The degree of reduction of myocardial MIBG activity was related to the distance covered. In a 160-km ultramarathon, reductions in left ventricular function were not significantly associated with changes in cardiac biomarkers [92]. After a 24-h ultramarathon, the stroke dimension and ejection phase indexes continued to decline within the last 6 h of the race but returned to the prerace level 2–3 days after the race [99]. Although the stress of an ultramarathon resulted in a mild reduction in left ventricular function and biomarker release, the mechanisms behind such consequences remain unknown $[92]$.

13.5.5 Ultra-running and the Immune System

 It is known that strenuous exercise is associated with tissue damage. This activates the innate immune system and local inflammation $[100]$. In experienced ultra-endurance runners, alterations in immunoglobulin concentrations after a race suggest an enhanced immune response. These alterations may have a role in the maintenance of subject health after an ultramarathon [100].

 Ultramarathoners often suffer postrace upper-respiratory-tract infections [101, [102](#page-11-0)]. In the "Two Oceans Marathon" in Cape Town, symptoms of upper-respiratory-tract infection occurred in 33.3 % of runners compared with 15.3 % of controls and were most common in those who achieved the faster race times [\[101](#page-11-0)]. The incidence in slow runners was no greater than that in controls

[101]. Vitamin C supplementation may enhance resistance to postrace upper-respiratory-tract infections that occur commonly in competitive ultramarathon runners and may reduce the severity of such infections [102].

13.5.6 Problems of the Locomotor System

 Ultra-running can cause minor problems to the skeletal muscle such as muscle soreness but also major problems to tendons and joints $[103-105]$. Different recent studies using MRI (magnetic resonance imagining) provided detailed analyses of the problems of the locomotor system such as bursal or presumed peritendineal fluid and/or edematous tissue, cartilage defects, or tibiotalar bone edema-like lesions [106].

 The main running-related musculoskeletal injuries in ultramarathoners were Achilles tendinopathy and patellofemoral syndrome [105]. However, it is even possible to run across a continent without an injury $[107]$. Despite the extreme nature and harsh environments of multiday ultramarathon races, the majority of injuries or illnesses are minor in nature $[103, 108]$ $[103, 108]$ $[103, 108]$. For example, during a 219-km five-day stage race, lower limb musculoskeletal injuries accounted for 22.2 %, predominantly affecting the knee $[109]$. In the 1005 km Sydney to Melbourne ultramarathon, 64 injuries were found in 32 runners [103]. The knee (31.3 %) and ankle (28.1 %) regions were most commonly injured. The most common single diagnosis was retropatellar pain syndrome, and Achilles tendinitis and medial tibial stress syndrome were the next most common injuries. Peritendinitis/tendinitis of the tendons passing under the extensor retinaculum at the ankle was common with 19 % of all injuries. In longer ultramarathons such as six-day race, Achilles tendonitis, patellofemoral pain, and tendonitis of the foot dorsiflexors were the three most common injuries $[110]$). In a 6-day race, the overall rate of injuries sufficiently severe to affect running performance was 60 $%$ [111]. In the "Trans Europe Foot Race" 2009, a 4487 km multistage ultramarathon covering the south of Europe (Bari, Italy) to the North Cape, an increase in the diameter of the Achilles tendon, intraosseous signals, bone lesions, and subcutaneous edema were found [104]. Interestingly, an increase of diameter of the Achilles tendon and bone signals were thought to be adaptive; subcutaneous edema and plantar fascia edema were related to abortion of the race $[104]$.

Conclusion

 Although we know a lot about physiology, anthropometry, training, and performance in these ultramarathoners, we do not know why these persons compete in these races, what motivates them, and why the number of master ultramarathoners increases across years.

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