Point: Counterpoint: Sickle cell trait should not be considered asymptomatic and as a benign condition during physical activity

**Point: Sickle Cell Trait Should Be Considered Asymptomatic and As a Benign Condition During Physical Activity**

Sickle cell trait (SCT) is found in ~8% of African Americans and may be found in up to 40% of West Africans. However, most of them are unaware of their status. This observation suggests that SCT may be asymptomatic and remains a benign condition for daily life activities (5). Indeed, numerous studies have reported that subjects with SCT had normal growth and development, normal morbidity (10) and mortality (21), and finally, normal life expectancy (12). Moreover, in worldwide countries of malarial endemicity, subjects with SCT have been found to be more healthy and able to perform heavy physical labor than subjects without the trait. Our hypothesis that SCT can also be considered asymptomatic and as a benign condition during physical activity is based on five kinds of data.

1) Epidemiological studies on large popular sporting events. Of 1,506 black males participating in the first Abidjan semi-marathon, SCT was detected in 123, i.e. 8.7%, a percentage similar to that observed in the general Ivory Coast population (15). Similarly, of 266 Cameroonian runners engaged in the International Mount Cameroon Ascent Race, SCT was found in 33 (12.4%), a prevalence similar to that of the ethnically corrected general population (25). These results suggest that, unlike in patients with symptoms or in an otherwise deleterious condition, there is no selective exclusion of individuals with SCT from participation in sports and physical activities.

2) Epidemiological studies on specific sports practitioners. Murphy (16) reported the presence of 39 (6.7%) subjects with SCT among the black football players in the National Football League. Similarly, 15 black high school athletes with SCT (10.5%) were observed by Diggs and Flowers (7). In physical education and sports colleges in Ivory Coast and Cameroon, the prevalence of SCT was reported to be 13.7% and 18.6%, respectively, i.e., a percentage similar to that observed in the general population of these countries (12%) and 17.3%, respectively; Refs. 13, 24). These studies suggest that SCT does not discourage its carriers from practicing high level competitive activities or from engaging themselves in sports-related professions. Moreover, there are subjects with SCT among champions and record holders. Among 129 national Ivory Coast champions or record holders in races during the 1956–1989 period, we found 13 athletes with SCT (10.1%; Ref. 14). Among 122 national Ivory Coast track and field throw and jump champions during the 1956–1995 period, 34 were found to have SCT (27.8%; Ref. 3). These percentages were similar and significantly higher than subjects with SCT in the general population of Ivory Coast. Athletes with SCT participated to the 1968 Mexico Olympic Games, as reported by Pearson (17). These data indicate that athletes with SCT are quite able to perform at the highest level of long-lasting and strenuous training.

3) Physical aptitude of subjects with SCT. Aerobic (maximal oxygen uptake and ventilatory threshold; Refs. 18, 27) and anaerobic (maximal anaerobic power; Ref. 2) metabolisms have been found similar in subjects with SCT and in controls with normal hemoglobin. However, blood lactate concentrations ([La]) during incremental exercise remain a controversial issue. Freund et al. (9) reported significantly higher [La] in SCT subjects than in controls. Unfortunately, these subjects exhibited significantly lower hemoglobin level than controls. In contrast, Gozal et al. (11) and Bilé et al. (3) found significant lower [La] in physical education students and sedentary subjects with SCT, respectively. Thiriet et al. (26) reported significantly lower [La] during consecutive anaerobic exercises in physical education students than in controls. Recently, Sura et al. (19) took into account the different bias of the above mentioned studies and measured [La] in the blood compartments of physical education students with SCT during incremental exercise and immediate recovery. They found no significant difference in whole blood, plasma, or red blood cell [La] between SCT carriers and control subjects with normal hemoglobin. Neither the red blood cell/plasma [La] ratio nor the plasmato-red blood cell lactate gradient differed between groups. Lactate distribution in the blood compartments did not differ between the two groups. These findings suggest that lactate production and/or clearance is quite similar during exercise in subjects with or without SCT. High [La] during exercise are associated with acidosis, which may, in turn, trigger sickle cell crisis. The observation of similar physical aptitude and similar or lower [La] in trained and untrained subjects with SCT during incremental (i.e., mainly aerobic) and anaerobic exercises is a key point to support our hypothesis that SCT should be considered asymptomatic and as a benign condition during physical activity.

4) Studies on exercise tolerance in subjects with SCT. The cardiac responses to exercise in children (1) and in men and women with SCT (8) were similar to those of control subjects. Cardiopulmonary and gas exchange responses to acute strenuous exercise at low altitude (1,270 m; Ref. 27), and, at moderate inspiratory hypoxia corresponding to simulated altitude of 2,300 m (28), were found comparable in healthy, black male basic recruits with SCT and in control subjects.

5) Follow-up of subjects with SCT engaged in official sports activities and military duty. During two seasons, the football and basketball squads of Melrose High School, which included students with SCT, participated in training programs and in competition without apparent disability that could be ascribed to the SCT (7). Similarly, a prospective and carefully controlled study on the effect of army basic training at an altitude of 1,270 m on SCT subjects failed to report any medical problem that could be directly attributed to SCT (29). Finally, an extensive epidemiological study on the nontraumatic deaths during U.S. armed forces basic training, 1977–2001, revealed that 26 deaths occurred in recruits with SCT. Interestingly, these 26 SCT deaths were all exercise related and due to congenital mitral valve disease, exertional heat illness, and idiopathic sudden death (20). One would thus suggest that none of the recruits with SCT died from a sickle cell crisis, i.e., due to SCT, and that the occurrence of idiopathic sudden death is inconsistent with the presence of symptoms.

Overall, SCT has to be reconsidered as a single-hemoglobin gene mutation. This means that subjects with SCT are similar for this gene, but that they may be different for all other hemoglobin genes. SCT associated with alpha-thalassemia is
not similar to SCT alone (22). Moreover, subjects with SCT may also be different with regard to all their remaining genes. New technologies in genomics and proteomics are revolutionizing the study of adaptation to environmental stress, particularly the adaptation to hypoxia and exercise (23). Of interest are the recent studies about the gene expression profiles of white blood cells (for the heat shock proteins) and skeletal muscle tissue in response to exercise and training stimuli, both showing many interindividual differences (5, 30). Together, these studies could explain some of the observations—exertional heat illness, training level of recruits—reported by Scoville et al. (20). Knowledge on human globin genes and their polymorphism shows that a mutation happens in a population and spreads because of its selective advantage (6). The HbS mutation occurred in regions of malaria endemicity and appeared to be, per se, asymptomatic and as a benign condition when the mutation arose (6).

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COUNTERPOINT: SICKLE CELL TRAIT SHOULD NOT BE CONSIDERED ASYMPTOMATIC AND AS A BENIGN CONDITION DURING PHYSICAL ACTIVITY

Sickle cell trait (SCT; or AS hemoglobinopathy) is the heterozygous form of sickle cell anemia and is present in over 2.5 million African Americans. Its prevalence can reach 20–40% in some areas of sub-Saharan Africa and 10% in the French West Indies (12). SCT is usually considered a benign disorder compared with sickle cell anemia...