Reply to Schumacher et al.

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TO THE EDITOR: The Letter to the Editor by Schumacher et al. (10) is well formulated but with no relevance for our studies (5, 8, 11) in which we aimed to pinpoint physiological factors that could lead to increased in exercise performance after altitude training. We specifically designed our study to separate the potential effects of hematological adaptations to hypoxia from other hypoxia-induced adaptations that could also lead to performance improvements. After 4 wk of live high-train low (LHTL), which at the time was assumed sufficient to induce hematological adaptations (7), subjects performed two \( \dot{V}O_2 \text{max} \) tests within a single day: 1) before blood manipulations and 2) 30 min after restoring plasma and red blood cell volumes to what they were prior to the intervention period. Less than 30 min after completion of the second exercise test, any red blood cells removed before the second \( \dot{V}O_2 \text{max} \) test were retransfused. The purpose for the retransfusion (i.e., normalization of blood volumes to what they were earlier on that specific day) was not to miss the opportunity to evaluate the potential time frame for LHTL to increase exercise performance in the following weeks. Thus it should be clear that the study participants experienced absolutely no athletic gain by participating in this specific part of our study, and as already stated in our manuscripts our studies were of course approved by the relevant ethical institutions, which includes a detailed description of all procedures and risks. As required, and as also described in the manuscripts, these were explained to all study participants. Furthermore, the specific above mentioned blood procedure was discussed with national antidoping authorities before initiation of the study. Finally, it should also be mentioned here that the intervention was discussed in detail with the authors of the Letter to the Editor (YOS, TP, CG) before the study was initiated.

When making use of substances/procedures in scientific studies potentially violating the World Anti-Doping Agency (WADA) code, the authors of the Letter to the Editor suggest prescribing “nonparticipation in competitions for a certain time after the intervention.” We believe this suggestion to be in error: 1) the time course for performance gains for any substance/procedure on the WADA list is unknown and likely also varies greatly from one individual to the other; 2) during a period of increased exercise capacity as induced by a forbidden substance/procedure also training intensity can be increased and hence further facilitate training adaptations. Some authors of the Letter to the Editor injected EPO for several weeks into athletes training up to 20 h/wk (9) to determine its effect on exercise performance, but they did not conform to their own suggestion by not informing the reader whether the volunteers were informed that they violated WADA rules and how this was dealt with. In similar studies (3, 6) by this group it is stated that the EPO-injected subjects “were not members of a national sporting squad,” but this does of course not exclude that the subjects were not license holders in organized sports (and hence underlying WADA rules). Since they are referred to as “recreational athletes” training up to 22 h/wk this could be the case. In other studies by this group there were no remarks as to how their potentially WADA violating studies were dealt with (1, 2, 9). According to the argumentation of the authors of the Letter to the Editor their studies could be interpreted as clear-cut doping. We assume they do not comply with this notion.

In the attempt to limit doping in organized sport it is important not to lose focus of what is relevant and what is not. It should be clear that to reduce, for example, the illicit use of autologous blood transfusion by athletes, for which no test is currently available (4), that humans—and preferentially athletes—will have to be blood transfused and closely monitored in well-designed scientific studies to establish reliable tests against its widespread practice. Luckily many WADA-funded research projects are indeed conducted with the inclusion of athletic populations as experimental volunteers and we highly approve of this notion. The question remains however, who is to decide who can participate in which studies without at the same time risking a ban from organized sport? Who has the supremacy—the local ethical committee or WADA? Would WADA sentence a person who is obliged to operate under their rules if at the same time participating in a scientific study where the euglycemic clamp technique (insulin is a WADA forbidden substance unless approved for medical needs) is applied? This will likely not be that case, but the example is no different from what we have applied in our LHTL study. And for the record—“yes”—we have been involved in such insulin clamp studies, and “yes” it is very likely that some of the included subjects may have violated WADA rules by doing so. Further complicating the matter is that national sport federations may constitute different rules. In some European countries, for example, the use of altitude tents, rooms, and trainers, which are frequently used in scientific studies, were forbidden for athletes but at the same time allowed in other countries. It could be considered whether WADA should officially grant permission for subjects to engage into WADA code-violating studies that have obtained local ethical approval to be conducted. This will not be an easy task however, and we fear that based on added bureaucracy and uncertainties regarding the time span for doping substances/procedures to affect exercise performance that such an approach would limit the scientific progress within the antidoping field.

The general skepticism toward the cocktail of science, doping, and sport is understandable. History has grim examples of scientists facilitating doping regimens to athletes, and it should be clear that a zero-tolerance policy toward scientists involved in any doping practice must be effectuated. This, however, becomes extremely difficult when an entire institution such as the Medizinische Universitätsklinik in Freiburg, Germany, is thrown into disgrace and mis-creditation simply because some medical doctors chose to systematically dope high-ranking...
athletes for years and years. It seems that the foul eggs have been picked out and that the University is now slowly recovering, but regaining the reputation as a trustworthy and established research institution is unfortunately not something that can be accomplished overnight. The harm done exceeds this by also affecting the entire scientific community, and it should be considered whether the publications (12, 13) involving the foul scientists and athletes—on which also some of the authors on the Letter to the Editor are coauthors—should be retracted. We are of the opinion that they should. We hope that the twisted picture presented by the authors of the Letter to the Editor, which could ultimately lead to a setback for future antidoping work does not discourage other established scientists from using state-of-the-art interventions, procedures, and study designs to address relevant scientific questions.

**DISCLOSURES**

No conflicts of interest, financial or otherwise, are declared by the author(s).

**AUTHOR CONTRIBUTIONS**

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**REFERENCES**