EFFECTIVENESS OF IMMUNOSTIMULATION IN ATHLETES

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INTRODUCTION

Illness remains a clinically important problem in sport because even a mild upper respiratory tract infection, gastrointestinal illness, or short febrile episode can disrupt training quality, reduced availability, and complicate return-to-play decisions. Athletes undertaking high training loads are exposed not only to repeated physiological stress but also to travel, crowding, sleep disruption, and psychological pressure, all of which may influence susceptibility to infection or the expression of illness symptoms[1,2]. For instance, in the 1-2 weeks following a marathon or an intensive training camp, athletes often show altered immune cell activity alongside higher rates of upper respiratory tract infections (URTIs).

Therefore, sports clinicians are frequently asked whether certain immune-support strategies can meaningfully reduce the number of infectious or illness episodes and symptom burden. Most preventative strategies include adequate energy/carbohydrate intake, sufficient protein for muscle recovery, good sleep hygiene, and basic infection control practices such as handwashing and avoiding sick contacts[2,3,4]. However, many practitioners have begun to consider additional strategies including immunostimulants; interventions intended to support or modulate immune function. The term immunostimulation implies a broad enhancement of host defense, yet in practice the goal is more modest: to preserve immune resilience, support mucosal and systemic responses, and reduce illness frequency or severity without compromising training adaptation or violating anti-doping rules[2].

This chapter reviews the practical evidence for immunostimulation in athletes with an emphasis on clinically relevant outcomes, including illness incidence, illness severity and duration, safety, implementation, and the relative position of supplements compared with foundational measures such as nutrition, sleep, hygiene, and vaccination.

EXERCISE-INDUCED IMMUNE CHANGES

Exercise induces rapid and highly dynamic changes in immune function. An acute bout of exercise induces rapid, intensity-dependent changes in leukocyte distribution and activity, mediated in part by catecholamines. Once exercise has ceased, a transient decrease in some lymphocyte subsets follows, particularly natural killer cells and effector T cells, while neutrophils may remain elevated for several hours[1,5]. Historically, these post-exercise responses were interpreted as evidence of an 'open window' of immune suppression during which infection risk was assumed to be increased.

That interpretation is now considered overly simplistic, with contemporary evidence indicating that many of the observed changes reflect redistribution of immune cells to peripheral tissues such as the lung, skin, and gut, where immune surveillance may be enhanced[5]. In other words, a reduction in circulating cells does not necessarily indicate reduced host defense. This shift in interpretation is important because it discourages the assumption that every hard session produces clinically meaningful immunosuppression.

Simultaneously, it would be equally misleading to conclude that heavy training does not impact immune function. Repeated prolonged exercise, especially endurance training performed with inadequate carbohydrate availability or low overall energy intake, can amplify stress hormone responses, alter inflammatory signaling, reduce salivary immunoglobulin A, and increase symptom reporting in the days after competition[1,2]. Illness risk appears to be

Illustration

greatest when high training loads coincide with additional stressors such as travel, poor sleep, crowding, environmental extremes, or rapid weight loss.

Accordingly, exercise should be viewed as an immune modulator that is generally beneficial at moderate doses but potentially disruptive when physiological and environmental stress accumulate[1,5]. Therefore, if illness vulnerability is driven primarily by an interaction between training stress and context, the goal of the clinician is not to indiscriminately 'boost' immunity, but to preserve normal immune competence while reducing the modifiable factors that increase the probability of illness expression.

FOUNDATIONAL MEASURES BEFORE IMMUNOSTIMULATION

The strongest interventions for maintaining immune health in athletes are not specialized supplements, as low energy availability, repeated training with depleted glycogen stores, inadequate protein intake, sleep restriction, and poor infection-control practices are more consistently linked with illness vulnerability than the absence of any nutraceutical. From a clinical perspective, the first step is therefore to identify modifiable contributors to recurrent illness, under-fueling, weight-loss practices, iron or vitamin D deficiency, excessive training monotony, insufficient recovery, or repeated exposure to infectious contacts.

Carbohydrate and Protein: Ingestion of carbohydrate before and during prolonged exercise attenuates rises in cortisol and some inflammatory mediators and may reduce the magnitude of acute immune perturbation. Adequate daily protein intake also supports recovery and immune cell function, however, extra protein above accepted sports nutrition targets has not been shown to further enhance immune function. These measures are best understood as preservation strategies, as they reduce the likelihood that normal training stress will be combined with a nutritional environment that undermines immune resilience[4].

Sleep and Hygiene: Athletes sleeping poorly, travelling across time zones, or living in close quarters with teammates are often exposed to non-training stressors that can outweigh the effects of most supplements[3]. Hand hygiene, minimizing contact with symptomatic individuals, attention to food and water safety during travel, and sensible management of training load during illness-prone phases should be treated as core immune-support measures rather than ancillary advice[2].

These foundational measures are worth emphasizing because supplement use can create a false sense of security. An athlete who is repeatedly under-fueled, accumulating fatigue, and sleeping inadequately is unlikely to derive durable benefit from an otherwise rational immunostimulatory strategy. The clinical yield is greater when supplements are layered onto good athlete management rather than as a substitute for it.

IMMUNOSTIMULATORY STRATEGIES

Once these fundamental measures are in place, selected immunostimulatory interventions may have a role in athletes. It is important to highlight that the quality of evidence differs substantially across interventions, and clinical enthusiasm should be proportional to that evidence rather than to marketing claims. The most useful framing is to separate strategies with consistent preventive evidence from those supported mainly by biological plausibility or small heterogeneous trials. Furthermore, it is important to limit unnecessary supplement stacking and keep the immunostimulant focus anchored to outcomes that matter in sport, fewer illness episodes, fewer symptom-days, lower illness severity, and less interruption of training and competition.

Probiotics

Probiotics currently have the most consistent supportive evidence among nutritional immunostimulants used in sport[2,6]. Their proposed mechanisms include modulation of the gut-lung axis,

improved barrier integrity, effects on mucosal immunoglobulin A, and altered inflammatory signaling. Across athlete studies, the clearest signal is a reduction in upper respiratory symptom severity, with some trials also showing fewer illness episodes or fewer days of symptoms.

The literature is heterogeneous because strain selection, dose, duration, and athlete population vary considerably[6]. However, utilizing probiotics as a preventive immunostimulant rather than therapeutic is the most justifiable interpretation. Emerging evidence supports the use of multi-strain products, containing Lactobacillus and Bifidobacterium species, administered daily over several weeks, rather than short term dosing once symptoms are observed. In practice, probiotics may be considered during winter training, tournament periods, overseas travel, or blocks of high-volume endurance training when illness burden has previously been problematic. Conversely, not all trials are supportive and findings cannot be generalized across products because probiotic effects are strain specific. Clinicians should therefore favor preparations with defined strains, transparent viable counts, and preferably athlete-specific trial data. In healthy athletes, safety is generally favorable, with gastrointestinal discomfort the most common adverse effect.

Bovine Colostrum and Beta-Glucans

Bovine Colostrum: Bovine colostrum has attracted interest because it contains immunoglobulins, growth factors, and bioactive peptides that may support mucosal immunity and gut barrier function[7]. Meta-analyses performed in trained or physically active populations suggest a modest reduction in upper respiratory illness burden, although the magnitude of effect is variable and mechanistic findings are less consistent. Most positive studies have involved endurance-trained individuals and supplementation periods of several weeks rather than days.

Beta-Glucans: These polysaccharides interact with innate immune receptors and may enhance aspects of host defense or reduce symptom burden during periods of heavy stress[8]. Endurance studies have observed fewer post-race respiratory symptoms and better self-reported wellbeing; however, some have shown little measurable effect[2]. Therefore, beta-glucans can be described as promising but not yet established.

Bovine colostrum and beta-glucans are better framed as second-line adjuncts for selected athletes rather than routine baseline recommendations for all squads. They may be reasonable during repeated high-risk phases, particularly in endurance populations, but current evidence does not support using them as universally.

Vitamins and Minerals

Micronutrient supplementation is generally advisable when it corrects a documented or strongly suspected deficiency.

Vitamin D: Supplementation is appropriate for both general health and immune support among deficient athletes and it is common in indoor athletes and during winter[9] However, routine vitamin D supplementation in already sufficient athletes has not consistently reduced respiratory illness burden. The practical implication is to routinely test Vitamin D levels and treat deficiency, while avoiding vitamin D supplementation as a universal anti-infection solution[10].

Vitamin C: In the general population it has limited preventive value, but in people exposed to brief periods of severe physical stress, including endurance athletes, regular supplementation has been associated with a lower incidence of common colds[11,12]. This

Illustration

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does not support year-round high-dose use, but it does support selective use during cold-weather expeditions, tournament congestion, stage racing, or intensive training camps.

Zinc: Evidence in athletes supporting zinc as a preventive immunostimulant for illnesses and infections is weak. However, zinc lozenges started at the onset of a cold may shorten symptom duration, thus it is more appropriately considered as an illness-management strategy than as a routine immunostimulant[13].

Other Micronutrients: Iron, selenium, magnesium, and B vitamins also contribute to normal immune function, and deficiency in any of these may compromise host immune defense[14,15,16]. However, routine high-dose supplementation in the absence of deficiency is not supported by current evidence and may introduce unnecessary risk or clinical complexity. Iron deficiency with or without anemia may impair both performance and immune competence. Selenium is involved in antioxidant defense and immune regulation, but excess intake can be harmful, with chronic over supplementation associated with gastrointestinal symptoms, and potential toxicity. Magnesium has important roles in cellular metabolism and neuromuscular function, yet direct evidence that supplementation enhances immune outcomes in otherwise sufficient athletes is limited. Similarly, B vitamins, particularly folate and vitamin B12, are essential for normal immune cell proliferation, but supplementation beyond correction of low intake or deficiency has not been shown to provide additional immunological benefit. Collectively, these additional micronutrients are best managed through dietary adequacy, targeted screening in at-risk athletes, and individualized replacement when clinically indicated.

Micronutrient supplementation should be approached with the same clinical rigor as any therapeutic intervention. Practitioners should provide correction where deficiency is identified or strongly suspected; however, in the absence of deficiency, claims of generalized immune enhancement should be interpreted with caution, particularly in the context of prolonged high-dose supplementation.

Herbal Extracts, Natural Products and Bacterial Lysates

Athletes commonly encounter products containing echinacea, ginseng, elderberry, medicinal mushrooms, or mixed 'immune blends'; and while mechanistic plausibility exists for several of these compounds, clinical data in athletic populations are sparse and inconsistent. Additionally, product standardization is poor, doses differ between trials, and positive findings often rely on small studies or mixed populations rather than athlete-specific cohorts[2].

Specifically, evidence supporting the use of echinacea, ginseng, quercetin, and mushroom-derived compounds remain inconclusive within the illness literature and robust athlete-specific efficacy has not been demonstrated[2,17]. These agents may be considered as adjunctive interventions in athletes who are already using them, provided product quality is assured, but they should not replace strategies with stronger evidentiary support. Bacterial lysates (e.g. OM-85) have a theoretical and clinical rationale in populations with recurrent respiratory infections, but direct evidence in healthy athletic cohorts remains limited[18].

VACCINATION

Vaccination is the most reliable immunostimulatory strategy discussed in this field because it prevents specific infections through well-established adaptive immune mechanisms[19,20]. Up-to-date influenza and COVID-19 vaccination are particularly important in athletes, given the consequences of respiratory outbreaks for training continuity, team availability, and travel logistics[19]. Vaccines differ from other immunostimulants in that their efficacy is not inferred from changes in indirect immune markers or symptom scores alone; rather, they demonstrate a direct and reproducible capacity to reduce disease incidence and severity for targeted pathogens.

From a practical standpoint, vaccination should be incorporated into annual medical planning[20]. Importantly, timing of vaccination should be considered as transient local or systemic side effects may occur, but these are minor compared with the consequences of infection during competition phases. Within an evidence hierarchy for illness prevention in sport, vaccination sits alongside foundational lifestyle measures and above most commercially marketed immune supplements.

Vaccination is especially relevant when athletes seek a single intervention with the highest probability of preventing time-loss illness. In that setting, keeping recommended vaccinations current is more defensible than relying on multiple low-certainty supplements, particularly

during periods of team travel or heightened community transmission of respiratory viruses.

SAFETY, DOSING AND ANTI-DOPING CONSIDERATIONS

Most of the supplements discussed have acceptable safety profiles when used appropriately, but the risk-benefit balance still deserves scrutiny. Specifically, fat-soluble vitamins and minerals can cause harm if chronically overused; zinc can cause gastrointestinal symptoms and interfere with copper status at high doses; and poor-quality supplements increase the possibility of contamination with substances prohibited in sport. None of the commonly used immunostimulants reviewed here are prohibited under the World Anti-Doping Agency (WADA) prohibited list*, but contamination remains a real practical concern.

A second implementation issue is dosing strategy, as many interventions that show benefit are administered daily and require several weeks before a clinically meaningful effect is apparent[2]. Consequently, clinicians should avoid presenting these products as immediate pre-event solutions. The more realistic model is planned use during anticipated high-risk periods, followed by review of individual response and continued use only if benefit is evident.

Third-party certification is not a peripheral consideration but a central component of clinical decision-making in elite and tested sport. Product quality should be weighted alongside efficacy data when evaluating supplementation strategies and interventions with limited manufacturing assurance may introduce disproportionate risk, including inadvertent anti-doping violations due to contamination with substances prohibited under World Anti-Doping Agency (WADA) regulations, thereby potentially outweighing any modest or theoretical benefit.

PRACTICAL IMPLEMENTATION

A pragmatic framework begins with screening for low energy availability, correctable micronutrient deficiency, recurrent heavy-load periods, travel burden, and sleep problems. The next step is risk stratification for potential immunostimulants. For example, endurance athletes with repeated winter URTIs or tournament athletes exposed to intense travel may be reasonable candidates for a probiotic supplement, while athletes with documented vitamin D deficiency should receive correction dosing and follow-up monitoring.

When a supplement is introduced, its intended purpose should be clearly defined. This may include reducing the incidence of recurrent upper respiratory symptoms during high-risk periods, supporting physiological resilience during intensified training phases, or attenuating the duration of established illness. Clearly delineating the objective minimizes indiscriminate supplement use and facilitates more accurate evaluation of effectiveness. Additionally, where not already in place, systematic monitoring of illness frequency, duration, severity, and associated training disruption should be implemented, as longitudinal tracking provides a more reliable assessment than subjective reporting alone.

An equally important consideration is recognizing when additional interventions are not required. Recurrent illness or infections in athletes presenting with low energy availability, menstrual dysfunction, unexplained fatigue, or progressive performance decline should prompt comprehensive clinical evaluation rather than escalation to multiple immunostimulatory agents. Immunostimulatory strategies are most appropriately applied as components of an integrated athlete management framework, rather than as compensatory measures for unresolved training or underlying health disturbances.

Finally, cost and practicality should also be considered, as some interventions require sustained daily use and may not be realistic across an entire squad. In those settings, targeted use in athletes with recurrent illness or in clearly defined high-risk phases is likely to be more efficient than universal supplementation.

GAPS AND CONTROVERSIES

First, illness outcomes in athlete studies are often based on self-reported symptoms rather than pathogen-confirmed infection, making it difficult to distinguish altered

Top 10 Practical Points for Clinicians

1. *Start with the basics: energy availability, carbohydrate timing, protein sufficiency, sleep, and hygiene have the strongest evidence base.*
2. *Interpret exercise-induced immune changes carefully; altered blood cell counts do not automatically mean clinically significant immunosuppression.*
3. *Screen for correctable contributors to recurrent illness, including vitamin D deficiency, iron deficiency, low energy availability, and excessive training load.*
4. *Use probiotics selectively for athletes with recurrent winter URTIs or during high-risk travel and competition periods; think in weeks, not days.*
5. *Consider bovine colostrum or beta-glucans only as adjuncts when the athlete remains illness-prone despite optimization of fundamentals.*
6. *Use vitamin D to correct deficiency, not as a universal immune supplement for already sufficient athletes.*
7. *Consider vitamin C during short periods of heavy physiological stress rather than as chronic year-round mega dosing.*
8. *Use zinc primarily as an early illness-management strategy, not as routine prevention.*
9. *Keep vaccinations current; this is the most dependable specific illness-prevention strategy in sport.*
10. *Use third-party tested products and review whether any intervention is actually reducing illness burden before continuing it.*

* WADA does not prohibit bovine colostrum; however, it advises caution due to its content of bioactive compounds, including insulin-like growth factor-1 (IGF-1), which is prohibited in sport. While available evidence suggests that commonly used doses (approximately 20–60 g/day) do not meaningfully increase circulating IGF-1 concentrations in healthy adults, the potential for contamination or unintended effects warrants careful consideration in tested athletes.

symptom perception from true changes in infection rate. Second, the probiotic literature remains difficult to synthesize because efficacy is strain-specific and formulations vary widely. Third, long-term safety and cost-effectiveness data for routine seasonal use of colostrum, beta-glucans, and mixed nutraceutical programs are limited.

Additionally, there remains ongoing debate regarding the extent to which exercise-induced immune suppression is overstated[1]. Contemporary perspectives suggest that, while heavy training represents a significant physiological stressor, observed immune alterations should be interpreted within the context of immune cell redistribution, inflammatory regulation, and the influence of non-training stressors. This has important practical implications, as strategies aimed at optimizing training load, recovery, and overall stress balance may be more effective for maintaining immune function than interventions focused solely on augmenting immune activity.

Future work should identify which athlete subgroups benefit most from specific interventions and should prioritize clinically meaningful outcomes, including missed training days, return-to-performance timelines, and athlete availability across a season. Trials that compare foundational lifestyle optimization with supplement-based strategies would be especially valuable, because they would more closely reflect the clinical choices faced by team physicians and performance staff.

CONCLUSION

Immunostimulation in athletes is best understood as a selective adjunctive strategy within a broader framework of athlete health protection. Exercise does alter immune function, but the clinical consequences depend on context, especially energy availability, sleep, travel, crowding, and overall training stress. Among supplemental approaches, probiotics currently offer the most consistent practical benefit, while colostrum and beta-glucans remain plausible but less certain. Micronutrients should be used to correct deficiency or for narrow evidence-based indications, and vaccination should remain central to preventive planning. A restrained, evidence-informed approach is therefore preferable to routine broad-spectrum supplementation.

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