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Exercise and Human Immunity in Adolescents (12–18 Years): Biomarkers, Sex Differences, and Evidence From Mexico and International Studies: a Narrative Review

Ejercicio e inmunidad humana en adolescentes (12-18 años): biomarcadores, diferencias de sexo y evidencia de estudios mexicanos e internacionales: una revisión narrativa

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Abstract

Purpose: To synthesize mechanistic and clinical evidence linking exercise to immune modulation, highlight key laboratory and clinical indicators, and summarize adolescent (12–18 years) data including sex differences and evidence from Mexico versus international studies. Methods: Narrative review focusing on meta-analyses/systematic reviews and primary studies reporting immune biomarkers (leukocyte subsets, salivary IgA, immunoglobulins, cytokines/interleukins) in relation to exercise intensity and volume in youth. Results: Consistent evidence indicates that regular moderate exercise improves immune surveillance and anti-inflammatory balance, reflected by transient mobilization of NK cells and T cells, higher salivary IgA, and lower chronic inflammatory markers (eg, CRP, TNF-α) in trained versus sedentary youth (1–5,8–12). Excessive load with inadequate recovery is associated with short-term susceptibility signals (eg, reduced salivary IgA) and higher illness burden in some athlete cohorts (3,9,15,26). Sex differences during adolescence may include stronger humoral responses in females and greater cytotoxic-cell mobilization in males, partly mediated by pubertal hormones (18–20). Evidence from Mexico remains limited but aligns with international patterns, particularly where obesity/inflammation and activity levels are assessed (28–30). Conclusions: Exercise is a potent, dose-dependent immunomodulator in adolescents. Periodized training with adequate recovery optimizes immune outcomes; screening for acute illness, energy deficiency, and overreaching is essential in youth sport.

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Resumen

Propósito: Sintetizar la evidencia mecanicista y clínica que vincula el ejercicio con la modulación inmunitaria, destacar indicadores clave de laboratorio y clínicos, y resumir los datos en adolescentes (12–18 años), incluidas las diferencias por sexo y la evidencia de México frente a estudios internacionales. Métodos: Revisión narrativa centrada en metaanálisis/revisiones sistemáticas y estudios primarios que reportan biomarcadores inmunitarios (subconjuntos de leucocitos, IgA salival, inmunoglobulinas, citocinas/interleucinas) en relación con la intensidad y el volumen del ejercicio en población joven. Resultados: La evidencia consistente indica que el ejercicio moderado y regular mejora la vigilancia inmunitaria y el equilibrio antiinflamatorio, lo que se refleja en la movilización transitoria de células NK y células T, mayores niveles de IgA salival y menores marcadores inflamatorios crónicos (p. ej., PCR, TNF-α) en jóvenes entrenados frente a sedentarios (1–5,8–12). Una carga excesiva con recuperación insuficiente se asocia con señales de susceptibilidad a corto plazo (p. ej., reducción de la IgA salival) y una mayor carga de enfermedad en algunas cohortes de atletas (3,9,15,26). Las diferencias por sexo durante la adolescencia pueden incluir respuestas humorales más fuertes en mujeres y una mayor movilización de células citotóxicas en varones, mediadas en parte por hormonas puberales (18–20). La evidencia procedente de México sigue siendo limitada, pero coincide con los patrones internacionales, especialmente cuando se evalúan obesidad/inflamación y niveles de actividad (28–30). Conclusiones: El ejercicio es un potente inmunomodulador dependiente de la dosis en adolescentes. El entrenamiento periodizado con recuperación adecuada optimiza los resultados inmunitarios; es esencial el tamizaje de enfermedad aguda, deficiencia energética y sobrecarga (overreaching) en el deporte juvenil.

Palabras claves: Adolescente, citocinas, ejercicio, inmunidad, leucocitos.

Introduction

The human immune system is dynamically regulated by metabolic and neuroendocrine signals. Exercise provides an acute stimulus that redistributes immune cells to peripheral tissues and enhances immune surveillance, while chronic training can shift baseline inflammatory tone toward an anti-inflammatory profile (5–7). Classic frameworks describe a dose-response relationship between exercise and infection risk, often presented as a conceptual 'J-curve' wherein moderate, regular exercise is associated with lower upper respiratory tract infection (URTI) burden, whereas excessive training or high intensity exercise, without adequate recovery can transiently increase susceptibility (1–4,9). In adolescents, these relationships interact with growth, pubertal maturation, and sex hormones, which may influence immune phenotypes and vaccine responses (18–20). This review summarizes the most influential evidence on exercise–immunity relationships, identifies clinical and laboratory indicators with strong associations to beneficial effects,

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discusses contraindications, and provides a Mexico-versus-international comparison with emphasis on 12–18-year-old athletes.

Methods

This manuscript is a narrative review intended for Pediatric Exercise Science. Evidence was prioritized from: (a) systematic reviews and meta-analyses examining physical activity or structured exercise and immune outcomes; (b) landmark mechanistic and consensus papers in exercise immunology; and (c) primary studies in youth (12–18 years) reporting immune biomarkers in athletes and sedentary comparators. Key outcomes included leukocyte subsets (neutrophils, lymphocytes, monocytes, eosinophils, basophils), NK cells, salivary IgA, serum immunoglobulins, and cytokines/interleukins (eg, IL-6, IL-10, TNF-α, IL-1β). Selection bias in the articles was carefully identified by examining the methodology used by the reviewed authors.

Strings were generated to identify articles with the studied variables through: ("exercise immunology" OR "physical activity")AND ("immune system" OR "immune function") AND infection. The inclusion criteria for the literature search included participants in the reviewed research of both sexes, aged 12 to 18 years, including cross-sectional and longitudinal observational studies, participants in physical exercise for health purposes, and high-performance athletes with different exercise intensities. The search focused on white blood cell lines and hematological biomarkers known as cytokines and interleukins. There was a 1887 articles obtained, of which 632 were related to the variables under investigation. No studies conducted in Mexico on this topic were identified.

Results

1. Clinical outcomes linked to exercise

Clinically, the most reproducible outcomes include reduced URTI incidence and severity among individuals engaging in regular moderate activity, and improved vaccine responses in some cohorts (1,2,6,21). In athletic contexts, illness burden is strongly influenced by training load, travel, sleep disruption, and energy availability, which can confound direct exercise effects (3,10,26,27).

2. Laboratory indicators with strong associations

Key laboratory indicators include: (a) transient mobilization of NK cells and effector T cells after acute bouts (6,7,12); (b) higher salivary IgA in well-recovered athletes compared with periods of heavy load (8,15,16); (c) lower chronic inflammatory markers (eg, CRP) and reduced pro-inflammatory cytokines with habitual activity (10,17,23,24); and (d) favorable cytokine balance characterized by increases in IL-10 and exercise-induced IL-6 signaling from skeletal muscle (5,7,10).

3. Effects across leukocyte lineages

Exercise can influence all five major leukocyte lineages. Moderate training tends to improve neutrophil function (chemotaxis, oxidative burst), promotes a more regulated monocyte/macrophage phenotype, and enhances lymphocyte and NK-cell trafficking and surveillance (6,12,13). Eosinophils and basophils are less consistently affected, with changes largely reflecting allergic status and acute stress responses (12–14).

4. Adolescents (12–18 years), athletes, and sex differences

Youth athlete studies indicate that immune adaptations depend on sport type, season phase, and recovery. In general, well-structured training is compatible with healthy immune profiles in adolescents, while intensive periods may reduce salivary IgA and increase illness symptoms in some cohorts (15,16). Sex differences during adolescence may involve stronger humoral responses in females and greater cytotoxic-cell mobilization in males, potentially driven by pubertal hormones and immunogenetic factors (18–20).

5. Evidence from Mexico versus international studies

Compared with international literature, Mexico-specific evidence directly measuring exercise-induced immune biomarkers in adolescents is scarce. However, Mexican studies addressing physical activity, obesity, and inflammatory risk factors support a pattern of lower inflammatory burden among more active youth, aligning with global evidence (28–30). More targeted studies measuring leukocyte subsets, immunoglobulins, and cytokines in Mexican adolescent athletes are needed. Priority national research lines include longitudinal immune monitoring across sport seasons, comparisons between school-based physical education and federated sport, sex- and pubertal-stage–stratified analyses, and integration of immune markers with cardiometabolic and academic outcomes.

Table1.
Indicators of variables, exercise intensity, and clinical significance

Indicator	Direction with moderate regular exercise	Risk signal with excessive load / low recovery	Notes / clinical relevance
Salivary IgA	Higher baseline; improved mucosal defense	Lower IgA; higher illness symptoms	Sensitive field marker in athletes (8,15,16)
NK cells (CD16+/CD56+)	Acute mobilization; enhanced surveillance	Blunted responses if overreached	Trafficking effect; interpret with timing (6,7,12)
CRP (hs-CRP)	Lower chronic low-grade inflammation	May rise with tissue damage/inflammation	Strong link to cardiometabolic risk (10,23,24)
TNF-α, IL-1β	Lower at rest with training	Can rise with systemic stress/infection	Pro-inflammatory cytokines linked to fatigue/illness (10,17)

IL-6 (myokine)	Acute rise with anti-inflammatory cascade	Excessive elevations with prolonged exhaustive bouts	Context-dependent; not purely pro-inflammatory (5,7)
IL-10	Higher anti-inflammatory balance	May be dysregulated in chronic stress	Marker of regulation and recovery (10)

Source: Author's own work

Table 2.
Potential implications of the findings for the world and Mexico

Domain	**International evidence (examples)**	**Mexico evidence (examples)**	**Age focus (12–18)**	**Main gaps**
Exercise immunology frameworks	Landmark reviews/consensus : J-curve, immune surveillance, athlete illness risk (1–4,9,10)	Adoption in curricula and clinical practice; limited direct biomarker cohorts	Indirect	Need Mexican cohort studies with standardized biomarker panels
Mucosal immunity (salivary IgA)	Athlete cohorts show IgA drops with heavy load; links to URTI symptoms (8,15,16)	Very limited pediatric athlete biomarker data published	Potentially	Seasonal monitoring in youth sport programs
Inflammation & cardiometabolic risk	Physical activity lowers CRP and inflammatory cytokines across ages (10,23,24)	Youth obesity/inflammation studies show activity-related differences (28–30)	Yes (some cohorts)	Need athlete vs non-athlete comparisons, immune-specific endpoints
Sex differences	Hormone-linked immune differences described (18–20)	Scarce Mexico-specific sex-stratified immune biomarker reports in athletes	Yes	Puberty staging and sex-stratified analyses

Source: Author's own work

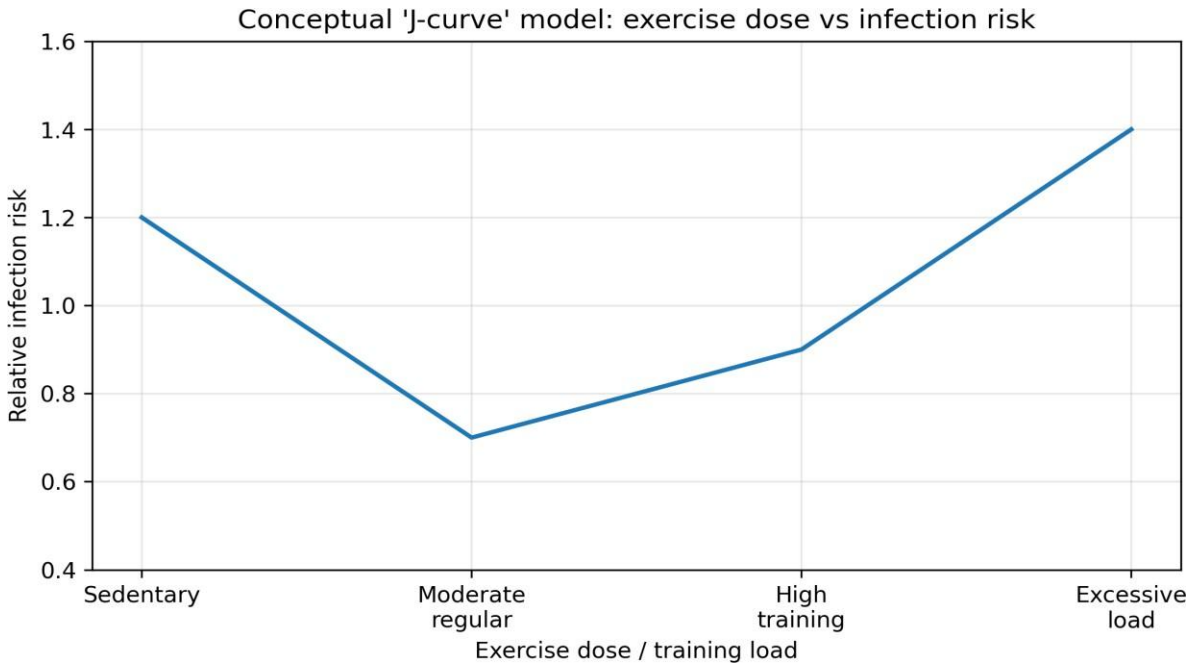

Figure 1.
Conceptual 'J-curve' model linking exercise dose to relative infection risk in youth and athletes.
Source: Author's own work

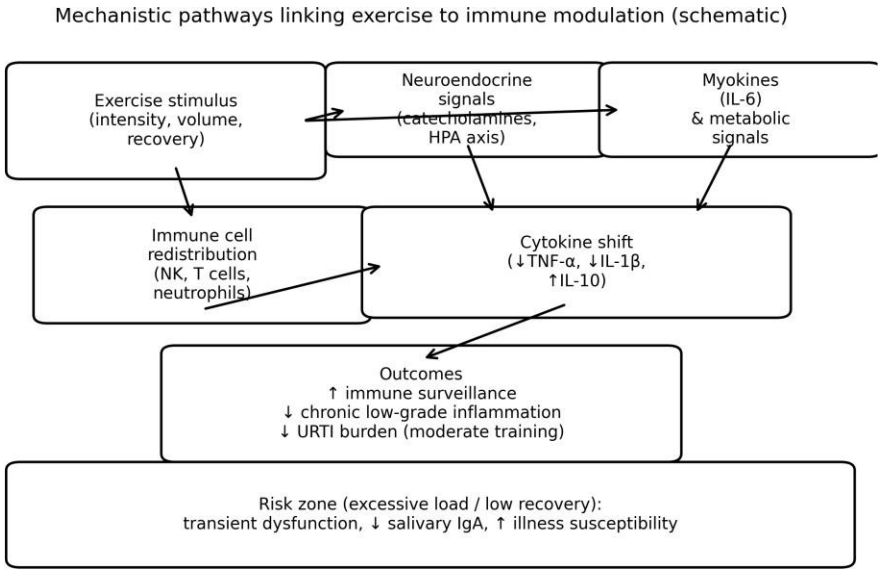

Figure 2.
Theoretical framework of the relationship to generate changes in immunity through the practice of physical exercise and sport.

Source: Author's own work

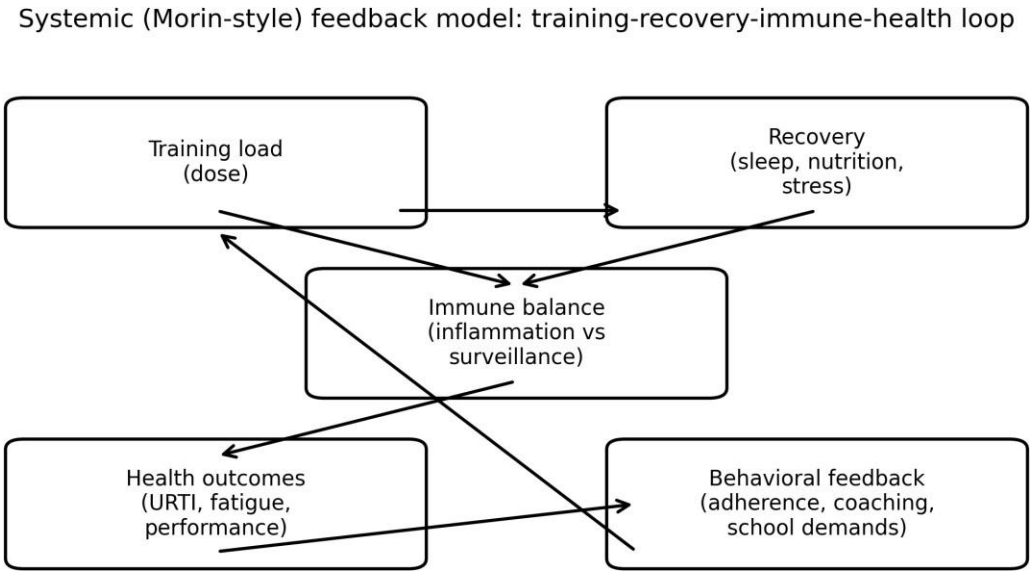

Figure 3.
Systemic (Morin-style) feedback model integrating training load, recovery, immune balance, and health outcomes.
Source: Author's own work

Discussion

Exercise intensity reflects the exerciser's perception of the activity, while workload is the objective measurement of the effort exerted. Thus, the exercise practice component, according to the reviewed articles, establishes the most important elements to relate to immunity in the reviewed articles that address the relationship between immunity, physical exercise, and sport.

The strongest evidence supports a dose-dependent immunomodulatory effect of exercise. Moderate regular exercise promotes immune surveillance and anti-inflammatory balance through neuroendocrine signaling, myokines, and immune-cell trafficking (5–7,10–12). In adolescents, structured training appears safe and potentially beneficial, but periods of excessive load related with intensity or volume of exercise, combined with sleep disruption, travel, or low energy availability may provoke transient susceptibility signals including reduced salivary IgA and increased illness symptoms (8,15,16,25,26,27).

For pediatric exercise science audiences, an important implication is that immune outcomes in youth sport are rarely determined by training load alone. Integrated monitoring that includes

wellness, sleep, nutrition, and illness symptoms improves interpretability of immune biomarkers (10, 25, 26,27). Sex differences should be considered when analyzing adolescent cohorts, ideally using pubertal staging and sex-stratified analyses (18–20).

Contraindications and safety considerations

Exercise should be temporarily withheld or modified in adolescents with febrile illness, acute systemic infection, uncontrolled asthma exacerbations, or signs of overreaching/overtraining. Screening for relative energy deficiency in sport (RED-S), inadequate micronutrient intake, and chronic sleep deprivation is recommended, as these factors can independently impair immune defenses (25,26).

Limitations

This is a narrative review and does not provide pooled effect sizes. Mexico-specific evidence directly linking exercise to leukocyte subsets, immunoglobulins, and cytokines in 12–18-year-old athletes remains limited, constraining country-level comparisons. Differences in assay timing, season phase, infection surveillance methods, and pubertal staging limit cross-study comparability. Priority national research lines include longitudinal immune monitoring across sport seasons, comparisons between school-based physical education and federated sport, sex- and pubertal-stage–stratified analyses, and integration of immune markers with cardiometabolic and academic outcomes.

Conclusions

Exercise is a potent and generally beneficial immunomodulator in adolescents when appropriately dosed and supported by recovery. Clinically useful indicators include illness symptom burden and salivary IgA trends in athletes, while laboratory markers such as leukocyte trafficking patterns and inflammatory cytokines provide mechanistic insight. Future Mexican studies should prioritize standardized biomarker panels, sex-stratified analyses, and longitudinal monitoring across sport seasons.

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