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Physical Activity in Autoimmune and Inflammatory Diseases: Mechanisms and Clinical Applications

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Abstract

Background: Inflammatory and autoimmune diseases are characterized by chronic immune dysregulation, systemic inflammation, and progressive functional impairment. Growing evidence suggests that physical activity may serve as an effective adjunctive therapeutic strategy in these conditions.

Aim: The aim of this review was to summarize current evidence regarding the immunomodulatory mechanisms and clinical applications of physical activity in inflammatory and autoimmune diseases.

Material and Methods: A narrative review of clinical trials, meta-analyses, and mechanistic studies published in recent years was conducted. The analysis focused on molecular pathways, immunological adaptations, and clinical outcomes associated with structured exercise interventions.

Results: Appropriately prescribed moderate-intensity physical activity modulates cytokine profiles, reduces pro-inflammatory mediators, enhances regulatory T cell (Treg) activity, and improves antioxidant capacity. Skeletal muscle functions as an endocrine organ, releasing myokines—particularly interleukin-6 (IL-6)- which exert anti-inflammatory effects via classical signaling pathways. Clinical evidence demonstrates that structured exercise programs improve pain, fatigue, functional capacity, and quality of life in patients with rheumatoid arthritis, axial spondyloarthritis, multiple sclerosis, systemic lupus erythematosus, inflammatory bowel disease, type 1 diabetes, and selected rare autoimmune disorders, without increasing disease activity.

Conclusions: Physical activity represents a safe and effective complementary therapy in inflammatory and autoimmune diseases. Personalized exercise prescriptions integrated with pharmacological treatment may enhance clinical remission, functional outcomes, and long-term disease management.

Keywords: physical activity; autoimmune diseases; inflammation; immunomodulation; rehabilitation

1. Introduction

In recent years, a significant shift has been observed in rheumatology and clinical immunology regarding the role of non-pharmacological interventions in the treatment of inflammatory and autoimmune diseases. Traditionally, it was believed that individuals with systemic connective tissue diseases should limit physical activity and avoid exertion in order to prevent disease exacerbations and the progression of joint and tissue destruction. These concerns stemmed primarily from the assumption that mechanical overload of the musculoskeletal system and the metabolic consequences of exercise might intensify inflammatory processes and worsen patients' clinical status. Over the past two decades, however, this view has undergone substantial revision. Findings from epidemiological, clinical, and molecular studies indicate that a sedentary lifestyle constitutes one of the key modifiable risk factors for health deterioration in patients with autoimmune diseases, affecting both disease activity and the development of systemic complications [1].

The change in previous management strategies results not only from the growing number of interventional studies, but also from a deeper understanding of the immunopathogenesis of autoimmune diseases. Contemporary immunology emphasizes the dynamic nature of the immune response and its close relationship with environmental and metabolic factors. Chronic low-grade inflammation, dysregulation of T and B lymphocyte responses, imbalance between pro- and anti-inflammatory cytokines, and abnormal activation of effector cells represent common features of many disease entities, such as rheumatoid arthritis, systemic lupus erythematosus, and inflammatory bowel diseases. In this context, physical activity is increasingly recognized as a potential modulator of immune responses through its influence on cytokine profiles, natural killer (NK) cell function, regulation of regulatory T lymphocytes, and the expression of myokines released by contracting skeletal muscles.

The scale of autoimmunity remains substantial and shows an increasing trend in many populations. An additional clinical challenge is the coexistence of multiple disease entities- two or more autoimmune diseases are diagnosed in a significant proportion of patients, complicating the clinical course, increasing the risk of organ complications, and intensifying psychological and social burden. This phenomenon, referred to as polyautoimmunity, requires integrated, multidirectional therapeutic strategies that include not only pharmacotherapy but also lifestyle interventions, rehabilitation, and psychosocial support. In this context, physical activity is no longer viewed solely as a recreational element but is increasingly regarded as an important component of supportive therapy, capable of modulating inflammatory processes and influencing immune system function [2].

Insufficient levels of physical activity among patients with autoimmune diseases remain common- it is estimated that the majority do not achieve the minimum levels of activity recommended by international health organizations. Contributing factors include chronic pain, fatigue, fear of disease exacerbation, reduced physical capacity, and the lack of individually tailored rehabilitation programs. A physically inactive lifestyle promotes the development of abdominal obesity, which constitutes a source of chronic low-grade inflammation. Visceral

adipose tissue exhibits endocrine activity, secreting pro-inflammatory adipokines and cytokines, including interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), which intensify the inflammatory cascade and may exacerbate symptoms of the underlying disease. This creates a pathophysiological feedback loop in which inflammation promotes physical inactivity, and inactivity further aggravates the inflammatory and metabolic components of the disease.

Regular physical activity provides benefits that extend beyond improvements in cardiorespiratory fitness. Appropriately prescribed moderate-intensity exercise has been shown to reduce levels of inflammatory markers, improve insulin sensitivity, decrease visceral fat mass, and normalize lipid profiles. At the immunological level, exercise is associated with increased production of anti-inflammatory cytokines, such as interleukin-10 (IL-10), and modulation of the hypothalamic–pituitary–adrenal axis, which may contribute to improved control of inflammatory responses. At the same time, physical activity positively affects psychosocial functioning, reducing symptoms of depression and anxiety, improving sleep quality, and enhancing patients' sense of self-efficacy in coping with chronic disease [3].

In light of the above evidence, it appears justified to consider physical activity as an integral component of comprehensive therapeutic management in inflammatory and autoimmune diseases. Nevertheless, further clarification of optimal training parameters—including type, intensity, frequency, and duration of exercise—is necessary in relation to the specific characteristics of individual disease entities and their activity phases. Integrating immunological, clinical, and rehabilitation perspectives allows for a more comprehensive understanding of the therapeutic potential of physical activity and provides a foundation for developing safe, effective, and personalized intervention programs. The aim of this review article is to present the current state of knowledge regarding the role of physical activity as a therapeutic component in inflammatory and autoimmune diseases, from immunological, clinical, and rehabilitation perspectives.

2. Molecular Mechanisms Underlying the Anti-Inflammatory Effects of Exercise

2.1. The Role of IL-6 and Myokine Signaling

Understanding how physical activity influences the immune system requires viewing skeletal muscle not merely as a structure responsible for locomotion, but as the largest endocrine organ in the human body. During contraction, muscle fibers release hundreds of biologically active molecules into the circulation—collectively known as myokines- which function as mediators of communication between the musculoskeletal system, metabolism, and the immune system [4]. These processes enable the transformation of a transient exercise stimulus into long-term anti-inflammatory and metabolic adaptations [5].

Interleukin-6 (IL-6) occupies a central and paradoxical position within this network, representing one of the most pleiotropic immune mediators. In clinical medicine, IL-6 is traditionally associated with the acute phase response, sepsis, and chronic inflammatory diseases, where elevated levels correlate with disease activity and tissue damage [6]. However, IL-6 released from skeletal muscle during physical exercise operates within a distinctly different, largely anti-inflammatory and metabolically beneficial framework. These differences arise from distinct secretion kinetics, tissue origin, and signaling mechanisms [7].

Feature	IL-6 as Pro-inflammatory	IL-6 as Exercise Myokine
Primary source	Macrophages, adipocytes, leukocytes	Skeletal muscle (no tissue damage)
Kinetics	Persistent, chronically elevated	Rapid increase, return to baseline 1-2 h
Signaling	Trans-signaling (binding to sIL-6R)	Classical signaling (binding to mbIL-6R)
Associated markers	Increased TNF-α, IL-1β, CRP	No TNF-α increase; elevated IL-10, IL-1ra
Main effect	Promotes inflammation, insulin resistance	Anti-inflammatory, enhanced fatty acid oxidation

Table 1: Comparison of IL-6 as a pro-inflammatory cytokine versus exercise-induced myokine

During prolonged aerobic exercise, there is a rapid and transient increase in muscle-derived IL-6 concentrations—up to approximately 100-fold above baseline levels. Importantly, this rise is not accompanied by a parallel increase in classical pro-inflammatory cytokines such as TNF-α or IL-1β. Such a response profile indicates that this is not a classical acute inflammatory reaction, but rather a specific physiological adaptive signal. In this context, IL-6 acts as an endocrine myokine, initiating a cascade of metabolic and immunoregulatory processes [8].

At the metabolic level, IL-6 enhances lipolysis and fatty acid oxidation, stimulates glucose uptake by skeletal muscle, and improves insulin sensitivity. These mechanisms are particularly relevant in the context of coexisting obesity, insulin resistance, and autoimmune diseases. Simultaneously, IL-6 induces the production of anti-inflammatory mediators such as IL-1 receptor antagonist (IL-1ra) and promotes the secretion of IL-10, while inhibiting the TNF-α response to endotoxin exposure. As a result, a single bout of exercise can trigger a cascade of secondary mechanisms that contribute to the resolution of inflammation [9].

A crucial distinction must be made between the two principal IL-6 signaling pathways. In so-called classical signaling, IL-6 binds to the membrane-bound IL-6 receptor (IL-6R), expressed primarily on hepatocytes, certain leukocyte subsets, and myocytes. This pathway predominates during the physiological response to exercise and is associated with metabolic and immunoregulatory effects. In contrast, trans-signaling occurs when IL-6 forms a complex with the soluble IL-6 receptor (sIL-6R). This complex can activate cells that do not express the

membrane-bound receptor, thereby promoting the persistence of chronic inflammation. This mechanism has been observed in conditions such as rheumatoid arthritis, obesity, and type 1 diabetes mellitus, in which IL-6 assumes a distinctly pro-inflammatory role [10].

Regular physical training leads to reduced resting concentrations of IL-6 and other markers of systemic inflammation. This effect is likely multifactorial. On the one hand, it results from the reduction of visceral adipose tissue, which itself constitutes a significant source of pro-inflammatory cytokines. On the other hand, it reflects repeated transient episodes of anti-inflammatory myokine release, which over time shift the immune system toward a more balanced response profile. In other words, short-term, controlled metabolic stress induced by exercise acts as a form of training for the immune system, enhancing its flexibility and regulatory capacity [11].

From the perspective of inflammatory and autoimmune diseases, this implies that IL-6 should not be viewed as a unidimensional marker of disease activity, but rather as a context-dependent mediator with dual functionality. Whether it contributes to the maintenance of inflammation or to its resolution depends on its source, duration of exposure, and signaling pathway. Appropriately prescribed physical exercise may therefore transform a potentially harmful cytokine into a driver of anti-inflammatory adaptation, representing one of the key molecular mechanisms underlying the therapeutic effects of physical activity in immune-mediated diseases.

2.2. Modulation of Lymphocyte Populations and Oxidative Stress

Physical activity exerts a significant impact on the cellular structure of the immune system and on the balance between pro- and anti-inflammatory processes. An acute exercise session induces mobilization of circulating NK cells and T lymphocyte subpopulations under the influence of catecholamines, while a post-exercise recovery period is characterized by temporary lymphopenia, effectively clearing the circulation of mature, more pro-inflammatory cells.

Chronic, moderate training promotes a shift in the cytokine profile toward a more anti-inflammatory state, characterized by increased IL-10 and decreased TNF-α and IL-6 at rest. Additionally, modulation of the Th1/Th2 and CD4/CD8 ratios has been observed, which is particularly relevant in older individuals and in autoimmune diseases such as multiple sclerosis (MS) and rheumatoid arthritis (RA).

T regulatory lymphocytes (Treg) play a key role in suppressing excessive immune responses, maintaining self-tolerance, and controlling inflammatory processes. Evidence from human studies and animal models suggests that regular exercise increases both the number and function of Treg cells, correlating with reduced disease activity in patients with MS and RA.

Simultaneously, physical activity affects the oxidative status of the organism. While intense exercise generates reactive oxygen species (ROS), regular moderate activity enhances endogenous antioxidant mechanisms, protecting cells from secondary oxidative damage. Through these mechanisms, systematic exercise not only attenuates chronic inflammation but also supports cellular homeostasis, which is crucial in the pathogenesis of autoimmune diseases [12,13].

3. Clinical Applications in Specific Autoimmune Conditions

3.1. Rheumatoid Arthritis: Kinesiotherapy Strategies and Clinical Effects

Rheumatoid arthritis (RA) is a chronic systemic disease characterized by symmetrical inflammation of the synovial membrane, leading to gradual and irreversible destruction of cartilage and bone. In the pathogenesis of RA, $CD4^+$ lymphocytes and macrophages play a central role, infiltrating joint tissues and secreting pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1, thereby sustaining chronic inflammation and driving structural joint damage.

Kinesiotherapy strategies for RA include low- to moderate-intensity aerobic exercises and resistance training, aiming to improve muscle strength, joint stability, and range of motion. Stretching and mobility exercises enhance tissue flexibility, reduce morning stiffness, and improve limb functionality. Exercise programs are often individualized based on disease severity, pain levels, and movement limitations.

Clinical studies demonstrate that regular physical activity in RA not only improves patient functional capacity and quality of life but also exerts immunomodulatory effects. Systematic exercise contributes to reduced pro-inflammatory cytokine levels, increased production of anti-inflammatory cytokines (e.g., IL-10), and favorable regulation of Th1/Th2 and Treg lymphocyte populations. Through these mechanisms, kinesiotherapy works synergistically with pharmacological treatment, supporting the reduction of disease activity and slowing the progression of joint destruction.

Current guidelines, including recommendations from Ontario Health and reviews by Holden et al., unequivocally identify physical exercise as a first-line conservative therapy in RA, emphasizing the importance of systematic implementation and monitoring for patient safety and tolerance [14,15].

3.2. Comparison of the Effectiveness of Different Forms of Physical Activity in RA

The selection of an appropriate form of physical activity in rheumatoid arthritis (RA) should be guided by specific therapeutic goals, taking into account both patient movement limitations and the desired clinical outcomes. A network meta-analysis (NMA) including 34 randomized controlled trials (RCTs) with a total of 2,435 participants allowed for a precise ranking of exercise modalities based on their clinical effectiveness in alleviating disease symptoms.

The analysis showed that Pilates is the most effective modality for reducing pain, as assessed by the Visual Analogue Scale (VAS), with a mean difference (MD) of −2.17 cm and a SUCRA value of 91.8%. The popularity of Pilates in RA stems from its low-impact nature combined with strengthening of stabilizing muscles, which effectively reduces pain and enhances functional comfort for patients.

For morning stiffness, the most effective intervention was combined training, integrating aerobic exercise (AE) with resistance exercise (RE), resulting in a mean reduction of 8.23 minutes and a SUCRA value of 100%. This combination of enhanced systemic circulation and mechanical stimulation of periarticular soft tissues promotes joint flexibility and improves early-morning functional performance.

Meanwhile, traditional Chinese exercises, such as Yijinjing, were most effective in reducing disease activity measured by DAS28-ESR (MD = −0.68; SUCRA = 95.5%). These practices

support gentle, systematic joint mobilization and improve autonomic regulation of the immune system, contributing to a decrease in systemic inflammatory activity in patients with RA.

These findings indicate that exercise selection in RA should be goal-oriented: Pilates is preferred for pain reduction, combined training for alleviating morning stiffness, and traditional Chinese exercises for modulating disease activity. Integrating these strategies into a comprehensive kinesiotherapy program enables a multidimensional improvement in clinical outcomes for patients with RA [16].

3.3. Impact on Inflammatory Markers and Physical Function

Although some meta-analyses suggest that physical exercise may not lead to immediate improvements in handgrip strength or short-term walking test performance, its beneficial effects on systemic inflammatory markers are indisputable. Regular physical activity in patients with rheumatoid arthritis (RA) has been shown to significantly reduce the erythrocyte sedimentation rate (ESR), with a mean effect size (ES) of −0.85, reflecting a decrease in overall systemic inflammation.

In addition, controlled mechanical loading of the joints during exercise stimulates chondrocytes to synthesize key components of the extracellular matrix, such as type II collagen and proteoglycans. This process enhances the structural integrity of the articular cartilage, increasing its resistance to further damage and slowing the progression of degenerative changes characteristic of RA.

From a clinical perspective, kinesiotherapy programs for RA patients should be carefully tailored to individual functional capacity and the current inflammatory status of the joints. Key practical recommendations include:

- Selection of low-impact exercise modalities: Activities such as swimming, cycling, or water walking reduce gravitational stress on the joints, minimizing the risk of overload and pain.
- Timing of exercise sessions: Physical activity should be scheduled for times of the day when pain is lowest and the effects of analgesic or anti-inflammatory medications are at their peak, enhancing comfort and adherence.
- Monitoring of patient response: If pain persists for more than 2 hours post-exercise, this signals the need to reduce the intensity or volume of subsequent sessions, preventing excessive joint strain and exacerbation of inflammation.

This approach allows for gradual improvement in physical capacity, supports joint function, and contributes to modulation of inflammatory activity, ultimately improving quality of life in patients with RA [17].

3.4. Axial Spondyloarthritis and Ankylosing Spondylitis: Physical Activity as a Cornerstone of Therapy

Ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) are chronic inflammatory diseases primarily affecting the sacroiliac joints and spine, leading to progressive stiffness, pain, and functional limitations. The updated 2022 ASAS-EULAR guidelines emphasize that optimal management requires a combination of pharmacological

therapy and comprehensive non-pharmacological care, in which patient education, regular physical activity, and physiotherapy constitute pillars of treatment equal in importance to medications. These interventions are aimed at controlling inflammatory activity, preventing structural damage, and maintaining quality of life [18].

Systematic reviews and meta-analyses of several dozen randomized trials have confirmed that various forms of exercise—from conventional kinesiotherapy and aerobic training, to stretching, Pilates, yoga, and supervised programs—significantly reduce disease activity (BASDAI, ASDAS), improve functional capacity (BASFI), and enhance spinal mobility (BASMI) compared with standard care or no exercise. In Polish studies and rehabilitation guidelines, emphasis is placed on a comprehensive approach combining daily kinesiotherapy with physiotherapeutic modalities. Whole-body cryotherapy administered immediately prior to exercise is particularly well-documented; its analgesic effects allow for increased range of motion. In randomized trials involving patients with AS, adding exposure to −110°C to an exercise program resulted in greater reductions in BASDAI scores and improvements in BASFI and spinal metric parameters compared with kinesiotherapy alone [19].

Aquatic exercise is recommended as a complementary approach, especially programs combining swimming with breathing and stretching exercises. Swimming styles that promote spinal extension and chest opening (e.g., backstroke) are preferred, as they facilitate correction of kyphotic posture and improve respiratory parameters. This was demonstrated in a six-month randomized trial by Nolte et al., which included swimming, land-based exercises, and respiratory training.

Digital solutions are also becoming an important component of modern therapy. Pilot studies using wearable technology (e.g., heart rate monitors) and online physiotherapy programs indicate that remote supervision can improve adherence to home exercise regimens and is associated with significant improvements in disease activity and functional outcomes compared with standard written instructions. An ongoing randomized trial, the Digital Functional Exercise Program (DFEP), based on inertial sensors and real-time feedback for patients with AS, is expected to provide further evidence on the long-term effectiveness of such interventions in maintaining spinal mobility [19].

3.5. Multiple Sclerosis: Neuroimmunological Modulation through Physical Activity

Multiple sclerosis (MS) is a chronic demyelinating disease in which physical activity (PA) demonstrates strong neuroprotective potential. For decades, patients with MS were advised to limit exercise due to concerns about exacerbating fatigue and triggering Uhthoff's phenomenon—a temporary worsening of neurological function in response to heat. Current evidence, however, indicates that appropriately dosed exercise is one of the most effective strategies to combat fatigue, which affects up to 80% of patients [20].

Recent studies reveal that physical activity induces significant neurobiological changes, notably through increased expression of brain-derived neurotrophic factor (BDNF). BDNF is a key neurotrophin responsible for synaptic plasticity, neuronal survival, and neurogenesis, particularly in the hippocampus. In individuals with MS, BDNF levels are typically reduced; regular aerobic and resistance training significantly elevate BDNF, supporting reparative processes in the central nervous system. Furthermore, high-intensity interval training (HIIT)

has been shown to reduce the neutrophil-to-lymphocyte ratio (NLR), reflecting attenuation of systemic inflammatory responses.

While the effect of exercise on overall brain volume (PBVC) as measured by MRI remains under discussion, phase 2 studies (2024) suggest that supervised physical activity may lower the annualized relapse rate and enhance functional connectivity within brain networks (rsFC), with direct benefits for cognitive performance and quality of life in MS patients.

FITT Guidelines and Harmonization of Recommendations

Contemporary MS guidelines, including those from the National MS Society and NICE (2024 update), emphasize regularity and progressive load adjustment. Harmonized recommendations enable precise dosing of exercise:

- Aerobic training: 2–3 days per week, 10–30 minutes per session, at moderate intensity (40–60% VO_2max).
- Resistance training: 2–3 days per week, 1–3 sets of 8–15 repetitions targeting major muscle groups.
- Dose–Response: A 2024 network meta-analysis indicated that the optimal weekly dose for reducing fatigue and improving muscular function ranges from 530 to 860 MET-minutes.

Resistance training lasting more than 8 weeks (minimum 3 sessions per week) has proven particularly effective in improving balance, as measured by the Berg Balance Scale (BBS), especially in patients with Expanded Disability Status Scale (EDSS) scores above 3.5 [21,22].

Individualization and Thermal Safety

Patient-centered principles in MS require exercise programs tailored to disability levels assessed via EDSS. For individuals with greater functional deficits, priority interventions include respiratory exercises (often using a spirometer), pelvic floor muscle training to improve bladder control, and functional electrical stimulation (FES). In Polish physiotherapy practice, promoted by initiatives such as Joanna Tokarska's Fizjopozytywni project, functional rehabilitation methods including PNF and NDT Bobath are emphasized for activating three-dimensional movement patterns.

To minimize the risk of overheating and Uhthoff's phenomenon, the Polish Society of MS Rehabilitation (PTSR) recommends:

- Exercising in cool, well-ventilated environments, preferably in the morning when energy levels are highest.
- Implementing interval-based rest periods (e.g., 15 minutes of exercise followed by 10 minutes of rest).
- Using cooling strategies, such as cooling vests or consuming cold beverages during sessions.
- Monitoring the "2-hour rule": if fatigue or pain persists for more than 2 hours post-activity, this signals that exercise intensity was excessive and requires adjustment.

By following these principles, exercise becomes a potent neuroimmunological intervention, enhancing both central nervous system resilience and overall functional capacity in patients with MS [23,24].

3.6. Systemic Lupus Erythematosus: Therapeutic Challenges and Recommendations

Systemic lupus erythematosus (SLE) is among the most complex autoimmune diseases, with the potential to affect virtually any organ system. The heterogeneity of clinical manifestations—ranging from mild cutaneous involvement to severe renal, cardiac, or neurological complications—has historically complicated the formulation of universal management guidelines. This challenge was addressed with the development of an international consensus, providing structured recommendations for the safe and effective implementation of physical activity in SLE patients [25].

Key Recommendations for Patients with SLE

The consensus emphasizes that physical activity is generally recommended for all patients with SLE, but careful consideration must be given to potential organ-specific contraindications, such as myocarditis, pericarditis, or active myositis. Exercise prescriptions should be individualized based on disease activity, organ involvement, and patient tolerance.

1. WHO Standards: For patients with inactive or mild disease, the target is 150–300 minutes of moderate-intensity activity per week, consistent with global guidelines for cardiovascular and musculoskeletal health.
2. Session Structure: Each exercise session should begin with a low-intensity warm-up to prepare the cardiovascular system and joints, followed by the main training component, and conclude with a "cool-down" phase incorporating stretching to reduce post-exercise stiffness and support musculoskeletal recovery.
3. Photoprotection: Due to the photosensitive nature of SLE, outdoor activity requires rigorous use of UV filters and protective clothing, as ultraviolet radiation is a well-documented trigger of disease flares.
4. Severe Thrombocytopenia: In patients with platelet counts below normal or those on anticoagulant therapy, contact sports are strictly contraindicated because of the elevated risk of internal bleeding.

Evidence from interventional studies indicates that supervised aerobic training in women with SLE improves cardiorespiratory fitness, reduces fatigue, and lowers circulating pro-inflammatory markers, including TNF-α, IL-2, IL-4, and IL-5, without exacerbating disease activity as measured by clinical indices [20]. Furthermore, exercise may enhance endothelial function, modulate autonomic balance, and support musculoskeletal health, all of which contribute to improved quality of life and long-term disease management.

Overall, the international consensus underscores that carefully dosed, supervised physical activity is both safe and beneficial for patients with SLE, provided that individual risk factors and disease-specific considerations are rigorously assessed and monitored. The integration of exercise into a multidisciplinary management plan—including pharmacotherapy, patient education, and lifestyle interventions—represents a cornerstone of modern SLE care [26].

3.7. Inflammatory Bowel Disease: Modulation of Clinical Course through Physical Activity

Inflammatory bowel disease (IBD), encompassing Crohn's disease (CD) and ulcerative colitis (UC), is a chronic inflammatory condition in which regular physical activity can modulate the clinical course by influencing intestinal barrier integrity, gut microbiota composition, and systemic inflammatory responses. Both animal models of IBD and clinical studies emphasize that moderate-intensity exercise promotes mucosal function, reduces inflammatory markers, and normalizes metabolic parameters, translating into better symptom control and decreased risk of extra-intestinal complications [27].

Regular, moderate physical activity enhances the diversity and stability of the gut microbiota, particularly promoting short-chain fatty acid (SCFA)-producing bacteria such as Faecalibacterium prausnitzii, Akkermansia, and members of the Prevotella genus. Higher abundances of these bacteria are associated with improved intestinal barrier integrity and anti-inflammatory effects. SCFAs, especially butyrate, strengthen epithelial tight junctions, modulate regulatory T cell responses, and suppress pro-inflammatory cytokine production—mechanisms that are particularly relevant in the context of chronic intestinal inflammation.

Skeletal muscle contraction during exercise induces the secretion of myokines, which, together with microbial metabolites, influence enteroendocrine L cells, promoting the release of glucagon-like peptides GLP-1 and GLP-2. GLP-2 enhances crypt proliferation and epithelial repair, while GLP-1 exerts anti-inflammatory and barrier-protective effects, as demonstrated in colitis models and preliminary clinical observations. The main mechanisms involved in the muscle–gut–microbiota axis—including GLP-1/GLP-2 release, accelerated intestinal transit, and reduction of visceral adipose tissue—and their potential relevance in IBD are summarized in Table 2 [28].

Mechanism	**Action in IBD**	**Final Effect**
GLP-2 release	Promotion of intestinal crypt proliferation	Accelerated regeneration of damaged mucosa
GLP-1 release	Inhibition of pro-inflammatory cytokines	Reduction of local inflammation
Increased motility	Shortened intestinal transit time	Reduced pathogen-mucosa contact
Adipose tissue reduction	Decreased cytokine pool from mesenteric fat	Attenuation of systemic inflammation

Table 2: Mechanisms of the muscle-gut-microbiota axis and their effects in IBD

Despite these benefits, prolonged high-intensity exercise (≥60 minutes at ≥70–80% VO_2max) should be avoided, as it can significantly reduce splanchnic blood flow, induce enterocyte hypoxia, increase I-FABP levels, and elevate intestinal permeability. Under such conditions, a "leaky gut" may develop, leading to translocation of lipopolysaccharides (LPS) into circulation,

increased pro-inflammatory cytokines, and elevated CRP, which may potentially trigger disease flares in patients with IBD, particularly in the presence of dehydration, hyperthermia, and sustained exercise stress.

A meta-analysis of 21 studies including 498 IBD patients demonstrated that structured exercise programs significantly improve quality of life (SMD 0.55; 95% CI 0.30–0.80) and markedly enhance aerobic capacity (SMD approximately 1.88), with only a modest, statistically non-significant reduction in short-term disease activity. Independently of effects on inflammatory biomarkers, regular physical activity is crucial for preventing osteopenia/osteoporosis and sarcopenia—conditions prevalent in a significant proportion of IBD patients. Osteopenia and osteoporosis affect 22–77% and 17–41% of patients, respectively, across different cohorts, while sarcopenia is observed in approximately 40–50% of patients, more commonly in CD. Resistance and aerobic exercise improve muscle mass and strength and may help maintain bone mineral density, mitigating the negative consequences of chronic inflammation and long-term corticosteroid therapy [27,28].

3.8. Type 1 Diabetes and Rare Autoimmune Disorders

Although type 1 diabetes (T1D) is primarily considered a metabolic disorder, its autoimmune basis makes physical activity an important immunomodulatory factor. Regular exercise in individuals with T1D has been shown to modulate levels of pro-inflammatory cytokines, including TNF-α and IL-6, potentially supporting control of the autoimmune process. Patients with T1D who engage in consistent physical activity exhibit a lower risk of developing autonomic neuropathy, nephropathy, and cardiovascular complications, as well as better glycemic control and reduced insulin requirements [29].

Resistance training in T1D patients can cause transient spikes in IL-6, particularly during high-intensity multi-joint exercises, which necessitates careful monitoring of blood glucose and inflammatory markers post-exercise. Individual responses to physical activity should also be considered due to variability in insulin sensitivity and the risk of hypoglycemia. Training programs of moderate intensity, combined with glucose monitoring before and after exercise, appear to provide the greatest benefits in improving cardiovascular function, muscle mass, and reducing markers of systemic inflammation.

For rarer autoimmune disorders, such as Sjögren's syndrome and systemic sclerosis (SSc), the role of physical activity is also significant, although research is more limited. In patients with SSc, exercise programs tailored to limitations caused by skin and joint stiffness improve grip strength, mouth opening, and finger flexibility, directly enhancing independence in daily activities. Aerobic exercise may additionally support cardiovascular health and pulmonary function, which is particularly important given the risk of lung fibrosis in this population.

In Sjögren's syndrome, resistance training and moderate-intensity exercise significantly reduce perceived pain and fatigue while improving overall physical capacity and quality of life. Programs combining both strength and functional exercises provide additional benefits in terms of muscle strength, joint mobility, and postural stability, which are crucial for maintaining independence in daily functioning [30].

4. Strategies for Managing Physical Activity During Disease Flares

The fluctuating course of autoimmune diseases requires continuous adaptation of physical activity plans by both patients and the healthcare team, taking into account pain levels, fatigue, and inflammatory activity. A key strategy is "pacing"—the deliberate regulation of effort and interspersing activity with short rest periods to avoid "boom-and-bust" cycles, in which periods of overactivity on "good days" are followed by significant symptom exacerbation. Systematic reviews indicate that pacing interventions in patients with chronic pain, fatigue, and rheumatic conditions lead to reduced fatigue, improved physical function, and greater sustainability of regular activity, particularly when combined with patient education and realistic goal-setting.

In clinical practice, pacing involves, among other strategies, planning the day according to a "time-contingent" approach (engaging in activity within predefined time blocks rather than continuing until pain occurs), breaking tasks into smaller modules, and consciously avoiding both complete inactivity and compensatory overexertion after periods of poor health. Additionally, incorporating short restorative breaks, breathing exercises, and light mobility exercises throughout the day can help maintain energy levels and improve overall well-being [31,32].

4.1. Protocol for Disease Flare Management

During a flare-up, characterized by increased pain, swelling, stiffness, and generalized fatigue, complete immobilization is not recommended unless there are acute cardiovascular, pulmonary, or neurological contraindications. Research in patients with rheumatoid arthritis (RA) and spondyloarthropathies shows that continuing gentle, adapted activity does not worsen disease activity and helps prevent functional decline.

In the acute phase, mild range-of-motion and stretching exercises for affected joints are primarily recommended, often performed as active-assisted or isometric exercises. The goals are to prevent contractures, maintain proprioception, and reduce the risk of thromboembolic complications while minimizing cardiovascular strain [32]. Aquatic exercises are also beneficial—warm water at approximately 32–34°C has analgesic and muscle-relaxing effects, and buoyancy allows movement with minimal joint loading. Studies in patients with RA and osteoarthritis show that this approach improves functional outcomes while maintaining good pain tolerance.

Relaxation techniques and therapeutic yoga, including breathing exercises, gentle postures (asanas), and mindfulness training, have been shown in randomized studies to significantly reduce fatigue, anxiety, and depressive symptoms in RA patients without increasing disease activity, likely through modulation of the stress axis and cortisol levels. After the most severe symptoms subside, a gradual return to the full exercise program is recommended. Typically, the first 1–2 weeks post-flare should involve no more than 50–70% of the pre-flare exercise volume and intensity, with further progression guided by patient tolerance and absence of symptom recurrence [33].

4.2. Safety Monitoring

Patient education should include recognition of warning signs that require modification or temporary cessation of activity. These include fever of unknown origin, new joint effusions, sudden asymmetric muscle weakness, pronounced resting dyspnea, or signs suggesting internal organ involvement (e.g., chest pain, palpitations). EULAR guidelines and expert recommendations emphasize the need for urgent medical consultation and temporary

suspension of more intense exercise until serious complications, such as myocarditis or thrombosis, are excluded.

Beyond alarm symptoms, patients should monitor subjective responses to activity, including pain and fatigue within 24–48 hours post-exercise, and respond to early signs of overexertion such as gradually increasing morning stiffness or decreased performance in daily activities. Hydration is essential, especially when taking disease-modifying drugs or NSAIDs, and maintaining good sleep hygiene is critical—research shows that 7–8 hours of sleep per night improves immune regulation and reduces pain and fatigue in rheumatic diseases [34].

5. System-Level Rehabilitation Framework and Institutional Recommendations

The effectiveness of exercise interventions in inflammatory diseases depends not only on the program itself but also on its integration into healthcare structures and close collaboration within a multidisciplinary team. EULAR recommendations from 2018 highlight that physical activity—meeting general public health guidelines (≥150 minutes of moderate-intensity activity per week plus strength training)—should be an integral part of standard care for patients with inflammatory rheumatic diseases. Planning of activity requires coordination among rheumatologists/immunologists, physiotherapists, rehabilitation physicians, and, when needed, psychologists and dietitians.

European and national guidelines emphasize the importance of initiating rehabilitative interventions early, at the time of diagnosis, to preserve professional and social functioning and reduce the risk of permanent disability. In the Polish healthcare system, health education is increasingly important, including training patients in self-monitoring activity, pacing strategies, and digital hygiene (limiting blue light exposure before bedtime), which improves sleep quality and indirectly enhances pain and fatigue control. Economic analyses cited by EULAR indicate that rehabilitation and physical activity promotion programs delivered within primary and specialized care are cost-effective—reducing hospitalizations, flare-ups requiring intensive therapy, and sick leave, thus generating measurable savings for both the healthcare system and the broader economy [34].

6. Conclusions and Future Perspectives

Physical activity in inflammatory and autoimmune diseases represents a highly effective therapeutic tool, with efficacy demonstrated at the molecular, cellular, and clinical levels. Through the release of anti-inflammatory myokines, modulation of regulatory T cell (Treg) activity, and optimization of antioxidant status, exercise can attenuate systemic autoimmunity, reduce chronic inflammation, and slow the progression of structural tissue damage.

Key conclusions for clinical practice include:

1. Safety first: Moderate physical activity, recommended at ≥150 minutes per week, is safe for most patients with autoimmune conditions, with a risk profile comparable to the general population. Appropriately prescribed exercise does not exacerbate disease activity and may reduce cardiovascular, metabolic, and musculoskeletal complications.

2. Modality specificity: Exercise selection should be tailored to the patient's clinical profile. Pilates is particularly beneficial for pain management and functional improvement in rheumatoid arthritis (RA), aquatic exercises enhance joint function and reduce load in spondyloarthropathies (SpA), and aerobic training is most effective for combating chronic fatigue in multiple sclerosis (MS) and systemic lupus erythematosus (SLE).
3. Need for professional supervision: Early stages of exercise programs should be conducted under the guidance of qualified professionals, particularly physiotherapists, to ensure correct technique, prevent overuse injuries, and adapt intensity to the patient's current functional and inflammatory status.
4. Education and adherence: Patient understanding of the benefits of physical activity is the strongest predictor of long-term therapeutic success. Education regarding pacing strategies, symptom monitoring, and coping techniques for pain and fatigue significantly improves adherence to regular exercise.

The future of exercise therapy in immunology is moving toward highly personalized programs based on patients' cytokine profiles, inflammatory status, and functional capacity. Wearable technologies and telemedicine enable real-time monitoring of inflammatory markers, heart rate, sleep quality, and activity levels, allowing dynamic adaptation of exercise regimens.

Integration of physical activity with modern pharmacotherapy, including biologic agents and JAK inhibitors, represents the most promising model of comprehensive care. Combining these approaches increases the likelihood of achieving full clinical and functional remission, improving quality of life and reducing the social and economic burden associated with chronic autoimmune diseases. On a global scale, systematic implementation of personalized exercise programs could substantially enhance health outcomes for millions of patients worldwide.

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REFERENCES

1. Sharif K, Watad A, Bragazzi NL, Lichtbroun M, Amital H, Shoenfeld Y. Physical activity and autoimmune diseases: Get moving and manage the disease. Autoimmunity Reviews. 2018;17(1):53-72. https://doi.org/10.1016/j.autrev.2017.11.010

2. Luo B, Xiang D, Ji X, Chen X, Li R, Zhang S, Meng Y, Nieman DC, Chen P. The anti-inflammatory effects of exercise on autoimmune diseases: A 20-year systematic review. J Sport Health Sci. 2024 May;13(3):353-367. https://doi.org/10.1016/j.jshs.2024.02.002

3. Liu Y, Mao S, Xie W, Qian G, Wu X, Xu H, Ossowski Z. Effect of exercise on abdominal obesity and inflammatory response in the older adults: a systematic review and meta-analysis of randomized controlled trials. Front Sports Act Living. 2026;7:1677087. https://doi.org/10.3389/fspor.2025.1677087

4. Ringleb M, Fabritius F, Godde J, Puta C, Bloch W, Javelle F. Circulating Myokine Responses to Acute Endurance Exercise and Their Role in Immunoregulation: A Systematic Review and Meta-Analysis. FASEB J. 2026 Feb 28;40(4):e71536. https://doi.org/10.1096/fj.202504780R

5. de Sousa CAZ, Sierra APR, Martínez Galán BS, Maciel JFdS, Manoel R, Barbeiro HV, Souza HPd, Cury-Boaventura MF. Time Course and Role of Exercise-Induced Cytokines in Muscle Damage and Repair After a Marathon Race. Front Physiol. 2021;12:752144. https://doi.org/10.3389/fphys.2021.752144

6. Nash D, Hughes MG, Butcher L, Aicheler R, Smith P, Cullen T, Webb R. IL-6 signaling in acute exercise and chronic training: Potential consequences for health and athletic performance. Scand J Med Sci Sports. 2023 Jan;33(1):4-19. https://doi.org/10.1111/sms.14241

7. Ringleb M, Fabritius F, Godde J, Puta C, Bloch W, Javelle F. Circulating Myokine Responses to Acute Endurance Exercise and Their Role in Immunoregulation: A Systematic Review and Meta-Analysis. FASEB J. 2026 Feb 28;40(4):e71536. https://doi.org/10.1096/fj.202504780R

8. Brandt C, Pedersen BK. The role of exercise-induced myokines in muscle homeostasis and the defense against chronic diseases. J Biomed Biotechnol. 2010;2010:520258. https://doi.org/10.1155/2010/520258

9. Dittmer D, Calzada-Nova G, Velazquez-Salinas L, Verdugo-Rodriguez A, Rodriguez LL, Borca MV. The role of interleukin 6 during viral infections. Front Microbiol. 2019;10:01057. https://doi.org/10.3389/fmicb.2019.01057

10. Nash D, Hughes MG, Butcher L, Aicheler R, Smith P, Cullen T, Webb R. IL-6 signaling in acute exercise and chronic training: Potential consequences for health

and athletic performance. Scand J Med Sci Sports. 2022;33(1):4-19. https://doi.org/10.1111/sms.14241

11. Teodoro TH, Costa KPM, Prestes J, Campanholi J, Navalta J, Pereira GB. The effects of acute and chronic exercise on immune markers of TH1/TH2 cells in older adults: a systematic review. Front Physiol. 2025;16:1453747. https://doi.org/10.3389/fphys.2025.1453747

12. Lu Z, Wang Z, Zhang XA, Ning K. Myokines May Be the Answer to the Beneficial Immunomodulation of Tailored Exercise—A Narrative Review. Biomolecules. 2024;14(10):1205. https://doi.org/10.3390/biom14101205

13. Ishida H, Ota H, Yanagida H, Dobashi H. An imbalance between Th1 and Th2-like cytokines in patients with autoimmune diseases--differential diagnosis between Th1 dominant autoimmune diseases and Th2 dominant autoimmune diseases. Nihon Rinsho. 1997 Jun;55(6):1438-43. Japanese

14. Feng W, Wang Y, Gu X, Yu D, Liu Z. Exercise as a modulator of systemic inflammation and oxidative stress biomarkers across clinical and healthy populations: an umbrella meta-analysis. BMC Sports Sci Med Rehabil. 2025 Nov 28;17(1):360. https://doi.org/10.1186/s13102-025-01327-8

15. Fu X, Zhang L, Wang C, Yue J, Zhu H. The effect of exercise therapy on pain, fatigue, bone function and inflammatory biomarkers individuals with rheumatoid arthritis and knee osteoarthritis: a meta-research review of randomized controlled trials. Front Physiol. 2025;16:1558214. https://doi.org/10.3389/fphys.2025.1558214

16. Zhang Y, He Z, Yin Z, Wang J, Gao W, Jie L. Effect of Exercise Interventions for Rheumatoid Arthritis: A Systematic Review and Network Meta-Analysis of Randomised Controlled Trials. J Pain Res. 2025 Sep 30;18:5109-5126. https://doi.org/10.2147/JPR.S537227

17. Harooni J, Pourjavid A, Amirkhizi F, et al. Combined healthy lifestyle score and odds of rheumatoid arthritis in Iranian adults: a nested case-control from PERSIAN Dena Cohort Study (PDCS). BMJ Open. 2025;15:e097715. https://doi.org/10.1136/bmjopen-2024-097715

18. Telkman M. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. Ann Rheum Dis. 2022. https://doi.org/10.1136/ARD-2022-223296

19. Liu X, Ji X, Hu L, Jiang T, Min A, Zeng L, Wang Y, Zhao M, Zhu J, Huang F, Weng C, Zhao Z. Effects of a Digital Functional Exercise Program on the Disease Activities and Physical Capabilities of Patients With Ankylosing Spondylitis: Protocol for a Randomized Controlled Trial. JMIR Res Protoc. 2025;14:e67556. https://doi.org/10.2196/67556

20. Alhusayni AI. A narrative review of clinical practice guidelines for the application of physical therapy and rehabilitation procedures in the management of multiple

sclerosis. Neurosciences (Riyadh). 2025 Oct;30(4):262-270. https://doi.org/10.17712/nsj.2025.4.20250054

21. Kim Y, Lai B, Mehta T, Thirumalai M, Padalabalanarayanan S, Rimmer JH, Motl RW. Exercise Training Guidelines for Multiple Sclerosis, Stroke, and Parkinson Disease: Rapid Review and Synthesis. Am J Phys Med Rehabil. 2019 Jul;98(7):613-621. https://doi.org/10.1097/PHM.0000000000001174

22. Alhusayni AI. A narrative review of clinical practice guidelines for the application of physical therapy and rehabilitation procedures in the management of multiple sclerosis. Neurosciences (Riyadh). 2025 Oct;30(4):262-270. https://doi.org/10.17712/nsj.2025.4.20250054

23. Blaess J, Geneton S, Goepfert T, Appenzeller S, Bordier G, Davergne T, Fuentes Y, Haglo H, Hambly K, Kinnett-Hopkins D, Su KY, Legge A, Li L, Mak A, Padjen I, Sciascia S, Sheikh SZ, Soriano-Maldonado A, Ugarte-Gil MF, Md Yusof MY, Parodis I, Arnaud L. Recommendations for physical activity and exercise in persons living with Systemic Lupus Erythematosus (SLE): consensus by an international task force. RMD Open. 2024 Apr 4;10(2):e004171. https://doi.org/10.1136/rmdopen-2024-004171

24. Kovács Z, Bacsur P, Kasza BB, Molnár T, Domján A. Physical Activity and Education in the Care of IBD: The Role of the Physiotherapist—A Narrative Review. J Clin Med. 2025;14(23):8602. https://doi.org/10.3390/jcm14238602

25. Finderle J, Schleicher VS, Schleicher LMS, Krsek A, Braut T, Baticic L. Exercise-Induced Modulation of the Gut Microbiota: Mechanisms, Evidence, and Implications for Athlete Health. Gastrointest Disord. 2026;8(1):1. https://doi.org/10.3390/gidisord8010001

26. Varghese S, Rao S, Khattak A, Zamir F, Chaari A. Physical Exercise and the Gut Microbiome: A Bidirectional Relationship Influencing Health and Performance. Nutrients. 2024 Oct 28;16(21):3663. https://doi.org/10.3390/nu16213663

27. Kasznár E, Csendes B, Gergő D, Hegyi P, Tóth R, Fogarasi A, Garami M, Ocskay K, Párniczky A, Obeidat M, Müller KE. Physical Activity Improves Quality of Life in Patients With Inflammatory Bowel Disease: A Systematic Review and Meta-Analysis. J Cachexia Sarcopenia Muscle. 2026 Feb;17(1):e70206. https://doi.org/10.1002/jcsm.70206

28. Varghese S, Rao S, Khattak A, Zamir F, Chaari A. Physical Exercise and the Gut Microbiome: A Bidirectional Relationship Influencing Health and Performance. Nutrients. 2024 Oct 28;16(21):3663. https://doi.org/10.3390/nu16213663

29. Herranz-López M, Agustín RM, Olivares-Vicente M, Pardines-Oltra L, Pino ACD, Bondia J, Rossetti P, Ampudia-Blasco FJ, Roche E. Patterns of circulating cytokines after 2 types of exercise in active type-1 diabetic patients. J Physiol Biochem. 2025 Nov;81(4):1335-1344. https://doi.org/10.1007/s13105-025-01123-5

30. Mitropoulos A, Jensen KY, Kouidi E, Boström C, Cuomo G, Diederichsen LP, Mattsson M, Hoekstra EM, De Vries-Bouwstra J, Dimitroulas T, Akil M, Jacobsen S, Klonizakis M. High-intensity interval and resistance training programme improves pain and fatigue outcomes in people with systemic sclerosis: a European multicentre randomised controlled trial. RMD Open. 2025 Nov 11;11(4):e005946. https://doi.org/10.1136/rmdopen-2025-005946

31. Barakou I, Hackett KL, Finch T, Hettinga FJ. Self-regulation of effort for a better health-related quality of life: a multidimensional activity pacing model for chronic pain and fatigue management. Ann Med. 2023;55(2):2270688. https://doi.org/10.1080/07853890.2023.2270688

32. Fu X, Zhang L, Wang C, Yue J, Zhu H. The effect of exercise therapy on pain, fatigue, bone function and inflammatory biomarkers individuals with rheumatoid arthritis and knee osteoarthritis: a meta-research review of randomized controlled trials. Front Physiol. 2025;16:1558214. https://doi.org/10.3389/fphys.2025.1558214

33. Zhang Y, He Z, Yin Z, Wang J, Gao W, Jie L. Effect of Exercise Interventions for Rheumatoid Arthritis: A Systematic Review and Network Meta-Analysis of Randomised Controlled Trials. J Pain Res. 2025 Sep 30;18:5109-5126. https://doi.org/10.2147/JPR.S537227

34. Barakou I, Hackett KL, Finch T, Hettinga FJ. Self-regulation of effort for a better health-related quality of life: a multidimensional activity pacing model for chronic pain and fatigue management. Ann Med. 2023;55(2):2270688. https://doi.org/10.1080/07853890.2023.2270688