THE EUROPEAN SOCIETY OF MEDICINE
Medical Research Archives, Volume 14 Issue 5

REVIEW ARTICLE

Paradoxical autoimmune-like manifestations in human immunodeficiency virus-infected patients: A clinical and immunological review

Brian Bernal-Alferes [1], Gustavo Linares-Liberato [2], Julio Martinez-Salazar [1]

[1] Centro Médico Nacional "20 de Noviembre", ISSSTE, CDMX
[2] Instituto Nacional de Rehabilitación "Luis Guillermo Ibarra Ibarra", CDMX

OPEN ACCESS

PUBLISHED
31 May 2026

CITATION
Bernal-Alferes, B., and Linares-Liberato, G., 2026. Paradoxical autoimmune-like manifestations in human immunodeficiency virus-infected patients: A clinical and immunological review. Medical Research Archives, [online] 14(5).

ISSN
2375-1924

ABSTRACT

Human immunodeficiency virus (HIV) infection is characterised by profound immune dysregulation and, paradoxically, by a broad spectrum of autoimmune and autoimmune-like manifestations, presenting a significant clinical challenge. Although antiretroviral therapy has transformed the prognosis of people living with HIV, immune restoration may unmask or amplify inflammatory and autoimmune phenomena, particularly through immune activation. This review synthesises the clinical and immunological mechanisms linking HIV infection with autoimmunity, including polyclonal B-cell activation, autoantibody production, molecular mimicry, loss of immune tolerance, regulatory T-cell dysfunction, chronic innate immune activation and altered cytokine signalling. We also review the main clinical phenotypes reported in people living with HIV, ranging from musculoskeletal, dermatological and connective tissue manifestations to vasculitic, haematological, and neurological involvement. These conditions frequently overlap with opportunistic infections, drug-related toxicity and non-AIDS comorbidities, creating important diagnostic and therapeutic challenges. Recognition of this paradox is clinically relevant because autoantibodies in HIV infection do not always indicate overt autoimmune disease, and immunosuppressive treatment must be carefully balanced against infectious risk, HIV control and immune status. A mechanistic understanding of HIV-associated immune dysregulation may improve diagnostic reasoning, guide symptom-directed evaluation and support safer management strategies for autoimmune-like complications in people living with HIV.

Abbreviations:

HIV: human immunodeficiency virus
TNF-α: Tumour necrosis factor-alpha
IL: Interleukin
RF: Rheumatoid factor
SpA: Spondyloarthritis
MAIT: Mucosal-associated invariant T cell
ILC3: Type 3 innate lymphocyte cell
Th17: T helper-17 cells
HLA-B27: Human leukocyte antigen B27 allele
MHC-I: Major histocompatibility complex class-I
SLE: Systemic lupus erythematosus
DILS: Diffuse infiltrative lymphocytosis syndrome
IgA: Immunoglobulin A
HIVICK: HIV-associated immune complex kidney disease
CD4 and CD8: Cluster of differentiation for helper T cells and cytotoxic T cells
iC3b: inactivated complement fragment cleaved from C3b opsonin
AAV: ANCA-associated vasculitis/ HCV:
Hepatitis C virus
IRIS: Immune reconstitution inflammatory syndrome
AIHA: Autoimmune haemolytic anaemia
AITP: Autoimmune thrombocytopenia
TMA: Thrombotic microangiopathy
TTP: Thrombotic thrombocytopenic purpura
aHUS: Atypical haemolytic uraemic syndrome
AIN: Autoimmune neutropenia
anti-ADAMTS13: antibodies against A disintegrin and metalloproteinase with a thrombospondin-type 1 motif, member 13
HLH: Haemophagocytic lymphohistiocytosis
MS: Multiple sclerosis
NMO: Neuromyelitis optica
anti-NMDAR: N-methyl-D-aspartate receptor antibody-mediated encephalitis
PML: Progressive multifocal leukoencephalopathy by reactivation of the John Cunningham (JC) virus
MACE: Major adverse cardiovascular events.

Introduction

Human immunodeficiency virus (HIV) infection is paradoxically associated with a broad spectrum of autoimmune manifestations, despite profound CD4+ cell immunosuppression. This paradox arises from complex immune dysregulation, including loss of regulatory T-cell function, polyclonal B-cell activation, molecular mimicry, and immune reconstitution phenomena. The prevalence of these autoimmune manifestations has risen, particularly with the widespread implementation of antiretroviral therapy, which, while beneficial in viral suppression, may inadvertently contribute to immune reconstitution inflammatory syndrome and other immune dysregulations. Most autoimmune conditions develop after HIV diagnosis, with a mean delay of approximately 10.6 years.

These manifestations encompass a range of conditions, from arthralgia and arthritis to bullous pemphigoid, psoriasis, and central nervous system HIV-derived encephalitis or HIV-associated neurocognitive disorders, with immune complex activation syndromes, autoimmune cytopenias, renal dysfunction, gland destruction, and cardiovascular repercussions, often presenting with diverse positive autoantibody titres, such as antinuclear antibodies and rheumatoid factor **(Figure 1)**.

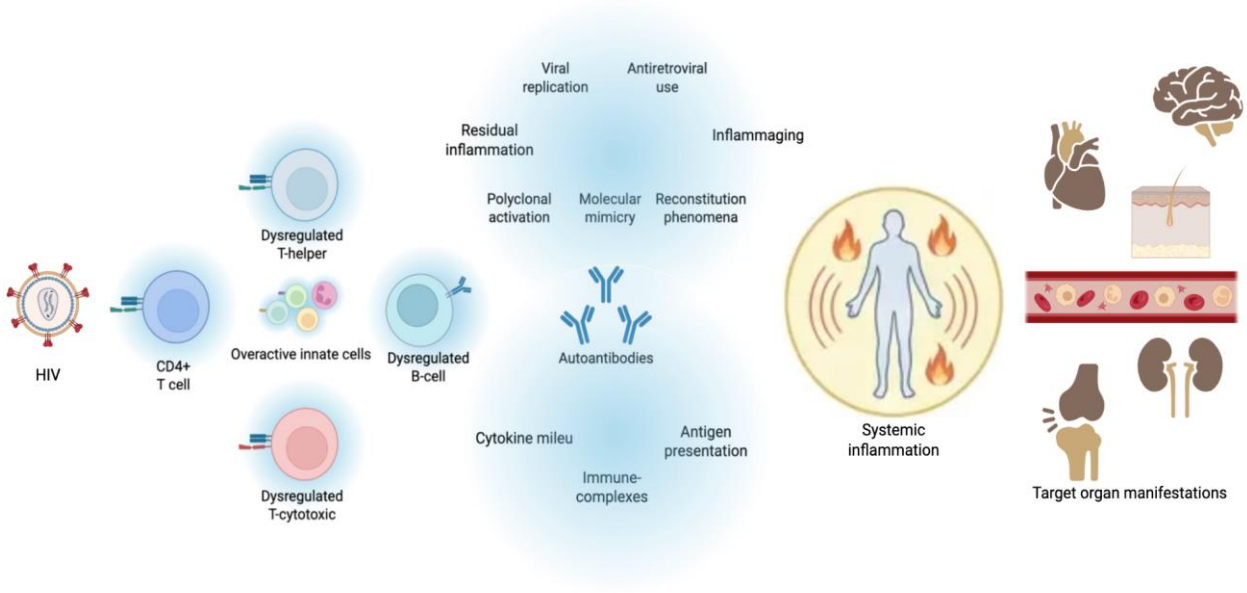

Figure 1: Autoimmune spectra of HIV-induced immune dysregulation and clinical manifestations

This increased prevalence of autoimmune disorders among HIV-infected patients is particularly notable following the restoration of T cell immunity facilitated by highly active antiretroviral therapy. While antiretroviral therapy has dramatically improved immune function and reduced opportunistic infections, a residual immune dysregulation syndrome persists in many HIV-infected individuals, characterised by heightened inflammation and T-cell activation, further increasing morbidity and mortality.[1]

ART normalises the autoantibody profile in HIV patients by decreasing CD33+CD11b+HLA-DR+ cells, which are associated with autoantibody production, while ART-naive patients have significantly higher levels and prevalence of elevated autoantibodies compared to

both healthy controls and HIV patients on ART.[2] Starting ART also lowers the amount of circulating immune complexes by lowering the amount of HIV antigen available, but it doesn't always stop the related autoimmune manifestations. In some instances, the initiation of ART and the subsequent restoration of the immune system can "unmask" or exacerbate autoimmune-like conditions through the immune reconstitution inflammatory syndrome.[2-4]

Further research into the chronic immune activation associated with HIV infection, characterised by elevated cytokine production, specific antigenic composition and new antibody-autoantigen binding with their interaction with Fc receptors on various immune cells, could elucidate the precise signalling pathways that drive this chronic inflammatory state and subsequent autoimmune organ damage sequelae.

Overview of Autoimmune-Like Manifestations in HIV

HIV replication during first contact causes CD4+ cell depletion, chronic innate immune activation, and B-cell hyperactivity that produces both clinical autoimmune diseases and preclinical autoimmune-like serologic phenomena without overt disease. Initially, serologic autoimmunity and B-cell overactivation cause a high autoantibody burden. Studies show that 45% of HIV patients have detectable autoantibodies, but only 12% have clinically relevant levels (ANAs ≥1:160, anti-dsDNA, anti-ENA, high-titre anticardiolipin/anti-β2GP1 ≥40 U/mL, or ANCA with PR3/MPO specificity). Antinuclear autoantibodies (ANA) are detectable in ~73% of ART-treated patients, often with fine-speckled/cytoplasmic patterns;[5] ANA and anti–smooth muscle antibodies are present in 43–23% of HCV/HIV coinfected patients.[6] Mechanisms include polyclonal B-cell activation, skewed immunoglobulin repertoires toward self-reactivity, and molecular mimicry between HIV proteins and self-antigens leading to immune complex formation.[7] Persistent immune activation and chronic inflammation drive immune dysregulation, T cell exhaustion, and senescence, contributing to the development of non-AIDS comorbidities, with or without concomitant infections such as tuberculosis-HIV coinfection.[8] Even with effective antiretroviral therapy, there is a described persistent immune activation, often termed 'residual immune dysregulation syndrome', which is characterised by increased T-cell activation and heightened inflammation, which correlates with elevated morbidity and mortality from conditions such as cardiovascular events, liver and kidney diseases, and malignancies.[1, 9, 10]

Chronic HIV-1 infection is characterised by persistent immune activation and inflammation, driving various B-cell abnormalities such as hypergammaglobulinaemia and the expansion of functionally impaired tissue-like memory B cells.[11] The paradoxical emergence of autoimmunity in HIV is attributed to immune imbalance, including polyclonal B-cell activation, loss of regulatory T-cell function, molecular mimicry between HIV proteins and self-antigens, and immune reconstitution inflammatory syndrome (IRIS) following antiretroviral therapy initiation. HIV also drives regulatory T-cell dysfunction, pyroptotic CD4+ loss, and CD8+ exhaustion, favouring persistent inflammation and loss of tolerance.[12] Importantly, 63-80% of autoimmune diseases occur in patients with CD4 counts above 200-350 cells, often in those with good virologic control on ART. Chronic activation and homeostatic T-cell expansion after ART initiation can promote autoantibody production and systemic autoimmunity.[13] Immune reconstitution inflammatory syndrome (IRIS) after ART initiation is strongly associated with new-onset or unmasked autoimmune diseases, including systemic lupus erythematosus, rheumatoid arthritis, immune-mediated myositis, sarcoidosis, various vasculitides, Still's disease and others.[14] People living with HIV have approximately 2.4 times the risk of developing autoimmune diseases compared to matched HIV-negative controls. The spectrum and severity of autoimmune manifestations often depend on the degree of immunosuppression and the stage of HIV infection **(Table 1.)**

Table 1: Major autoimmune-like syndromes and mechanisms in HIV

Manifestation group	HIV association	Key immune mechanisms
Arthralgia/arthritis	HIV chronic arthralgia syndrome, HIV-associated arthritis, septic arthritis, Rheumatoid arthritis	Immune activation, TNF-α, IL-6, and IL-1β predominance, joint susceptibility to infection, B-cell dysregulation with RF production
Spondyloarthritis	Ankylosing spondylitis, Reactive arthritis, psoriatic disease, undifferentiated SpA	Aberrant innate MAIT, ILC3, γδ T cells and Th17 responses, HLA-B27-independent enthesitis. Increased gut-joint axis.
Inflammatory myopathies	Dermatomyositis, inclusion body myositis	Interferon upregulation, sarcomere MHC-I overexpression
Systemic immune-complex disease	SLE-like disease, DILS, SLE nephropathy, bullous pemphigoid, IgA vasculitis, HIVICK	Loss of tolerance, molecular mimicry, CD4/CD8 imbalance, aberrant immune complex depuration with aberrant iC3b function

Manifestation group	HIV association	Key immune mechanisms
Vasculitides	Cutaneous purpura, large-vessel vasculitis, aortoiliac vasculopathy, Takayasu's arteritis, polyarteritis nodosa, Behçet-like syndrome, AAV, essential cryoglobulinaemia	Direct vessel vasculitis cytotoxicity, Behçet-like endothelial immune complexes, HCV-complex and HIV mimicry, and IRIS.
Intravascular hematotoxicity	AIHA, AITP, TMA (TTP or aHUS), AIN	Cell-specific directed cytotoxic complement-activating autoantibodies, anti-ADAMTS13, bone marrow suppression
Hyperinflammation	Secondary haemophagocytic lymphohistiocytosis	Macrophage cytokine storm activation, viral, fungal or bacterial opportunistic trigger, HLH-IRIS
Central nervous system	MS/NMO, anti-NMDAr encephalitis, HIV neurocognitive disorders	Loss of immune privilege/ignorance, JC virus opportunistic reactivation (PML), CNS-IRIS, HIV-associated neurocognitive disorders.
Cardiovascular	Autoimmune myocarditis, HIV-cardiomyopathy, pericarditis and pericardial effusion, MACE, antiphospholipid syndrome	Cardiac autoantibodies, pericardial immune infiltration, accelerated inflammatory atherogenesis, antiprothrombin, anticardiolipin and lupus anticoagulant

Rheumatologic and connective tissue disorders associated with HIV infection

The key paradoxical clinical autoimmune manifestations in HIV include musculoskeletal and systemic manifestations commonly seen in HIV infection. The prevalence of musculoskeletal symptoms in HIV-infected individuals ranges from 10% to 45%, with articular manifestations being particularly frequent. The reported frequency of arthralgia, often moderate and oligoarticular, approaches 35% of cases, with knees, shoulders, and elbows being predominantly affected.[15] The underlying mechanisms contributing to persistent inflammatory states within the musculoskeletal system in HIV-infected individuals are often attributed to ongoing adaptive immune B- and T-cell imbalances and cellular senescence.[16] HIV-associated arthritis often mimics rheumatoid arthritis and spondyloarthropathies (notably reactive arthritis and psoriatic arthritis), while systemic lupus erythematosus-like syndromes and Sjögren's syndrome have also been documented, presenting diagnostic and therapeutic challenges.[17, 18] B- and T-cell dysfunction observed in HIV infection contributes to the development of subclinical disease, akin to inflammatory autoimmune arthritis. Due to the overlapping symptoms with opportunistic infections and drug toxicities, the many HIV autoimmune-like manifestations should have a complete diagnostic work-up.

Arthritis in HIV-infected individuals sometimes presents with atypical presentations and may have an intermittent course with painful joints.[19] During the evaluation according to the stage of the HIV infection, the first differential in monoarthritis should be septic arthritis. Synovial fluid analysis, when available, should be performed with microbial cultures.[20]

Rheumatoid arthritis shows a modestly elevated risk (adjusted hazard ratio of 1.51) of developing in HIV-infected patients. Conversely, HIV infection can influence the clinical presentation and progression of patients already diagnosed with rheumatoid arthritis.[21] Of note, the presence of rheumatoid factor in the serum of patients suspected of HIV infection might cause false-positive HIV serology, and ELISA seems to be a more specific test for detecting HIV in patients with positive rheumatoid factor.[22] The depletion of CD4+ lymphocytes due to HIV conveys a loss of tolerance and autoimmune activity that sustains rheumatoid arthritis, resulting in an HIV and arthritis synergy. An HIV-infected patient exhibiting rheumatoid arthritis-like symmetrical polyarthritis may present with severe, transient pain lasting from 2 to 24 hours in the absence of synovitis or other inflammatory indicators. Most of the time, larger joints are affected, but smaller ones like the metacarpophalangeal joints could also be involved. The emergence of rheumatoid arthritis can be exacerbated by immune reconstitution following highly active antiretroviral therapy, while serological abnormalities like rheumatoid factor and antinuclear antibodies are commonly observed, though rarely clinically significant.[23] Post-ART arthritis with seropositive rheumatoid factor commonly appears as a polyarticular flare due to residual inflammation from the formation of circulating immune complexes (anti-Fc idiotypes or anti-HIV antigens) and a low rate of complement (C3bi) complex depuration despite viral suppression. The presence of anti-cyclic citrullinated peptide (ACPA) antibodies has rarely been explored in HIV studies, although increased rates of ACPA have been reported as high as 15% in HIV patients not taking cART; these rates may drop to <6% after 6 months of treatment with cART.[24]

Spondyloarthritis (SpA) is an umbrella term for a heterogeneous group of inflammatory rheumatic diseases affecting axial and peripheral joints and entheses with a seronegative profile, often presenting in HIV individuals as ankylosing spondylitis (AS), reactive arthritis (RA), or psoriatic arthritis (PsA). AS is rare in the general population and seems to be similarly unusual in HIV-infected patients. AS, most recently known as

radiographic axial SpA (r-axSpA), has features of inflammatory back pain, HLA-B27 positivity and radiographic sacroiliitis, and some authors have suggested that the immunological mechanisms driving AS are not only dependent on CD4+ T cells, such as Th17, but also more influenced by innate IL-17 secreting cells, biomechanical stress, and microbiome interactions which are mainly altered during HIV infection.[25] These conditions often exhibit an atypical course in HIV-infected patients, sometimes lacking characteristic radiographic changes or presenting with unusual extra-articular manifestations, such as inflammatory bowel disease and increased cancer burden, often necessitating nuanced diagnostic approaches to differentiate them from opportunistic infections or other HIV-related complications.[26]

Reactive arthritis can occur in HIV-infected patients who have acquired urethral or gastrointestinal infections. The reported frequency of reactive arthritis has ranged from 0.5 to 9.9% in HIV-positive patients, with most cases manifesting as an incomplete triad form and a similar prevalence of HLA-B27 positivity. HIV infection per se does not increase the risk; rather, susceptibility to reactive arthritis in this context may reflect the high-risk behaviours associated with HIV acquisition. The condition is triggered by various organisms, particularly those causing sexually transmitted infections. Since the HIV epidemic, high-risk sexual practices have become more restricted, resulting in reduced transmission of arthritogenic urogenital and enteric pathogens. Despite this, reactive arthritis remains a prevalent joint manifestation in HIV-infected patients. Reactive arthritis and HLA-B27-negative-associated arthritis, conjunctivitis and urethritis are driven by gut dysbiosis and microbial translocation fuelling IL-23/IL-17 via innate sensing (e.g., NOD-like receptors) and heightened antigen presentation.[27] The "leaky gut" concept is propagated with ongoing HIV viral replication.[28] HIV replication continues in CD4+ gut-associated lymphoid tissue (GALT), and even with ART, the depleted Th17 cells do not restore their cellular levels, which makes it harder for the gut mucosal barrier to heal and for microbial products to be cleared, further expanding possible arthritogenic peptide presentation.[29, 30]

Psoriatic arthritis (PsA) or psoriatic disease (implying a more extensive definition beyond skin and joint pathology) is a common comorbidity also observed in the HIV-infected population, often presenting with more severe and persistent symptoms.[32] PsA represents a high prevalence of inflammatory arthritides in HIV-infected patients, presenting with atypical symptoms that mimic rheumatoid arthritis and exacerbate during post-ART immune reconstitution. The estimated prevalence rates of psoriatic arthritis (PsA) were found to be between 0.02 and 2%.[32] Specifically, HIV-infected individuals with PsA frequently exhibit more severe and persistent skin lesions, often presenting with guttate, inverse, and erythrodermic subtypes. The arthritic manifestations, such as oligoarthritis or polyarthritis, can be particularly severe and refractory to conventional treatments. This heightened severity in HIV-positive individuals is likely influenced by the profound immunosuppression which predisposes to a paradoxically heightened CD8+ T cell immune response.[33] This complex interplay between immunosuppression and immune activation contributes to the exacerbated clinical manifestations of PsA. Nonetheless, arthritis mutilans and axial PsA patterns remain an uncommon manifestation within the spectrum as compared with HIV-negative patients.[34, 35]

These chronic inflammatory joint processes involve a range of comorbid conditions and complicate management due to diagnostic overlap with infections or drug toxicities. HIV-associated arthritis is typically oligoarticular and additive and can be unmasked or worsened by immune recovery. Persistent innate activation via microbial translocation, monocyte/macrophage dysregulation, and elevated IL-23, IL-17, TNF-α, IL-6, and IL-1β cytokines driving synovial inflammation contribute to arthritis immunopathology.[33-34] Meanwhile, extra-articular involvement is frequently due to the systemic cytokines related to a senescence phenotype milieu of immune-associated activation by HIV proteins and inflammaging.[35] The occurrence of manifestations in the joints and enthesis of typical SpA, skin and nail inflammation similar to PsA or other non-specific organ involvement with no clear or complete criteria is often termed 'undifferentiated SpA'. The myriad of manifestations with fatigue and debilitating flares, no objective synovitis and Achilles tendinitis, dactylitis or plantar fasciitis and polyenthesitis and osteitis on imaging are often the presenting clinical course of undifferentiated SpA in HIV-infected patients.[36]

Inflammatory myopathies, including dermatomyositis and inclusion body myositis, manifest with distinctive clinical features in HIV-infected patients.[37] HIV-associated myositis is clinically and histologically indistinguishable from inflammatory myositis and generally has a favourable prognosis, responding well to immunosuppressive therapy and even resolving spontaneously.[18] Sustained type I interferon secretion drives the chronic immune activation that underlies autoimmune inflammatory myopathies in HIV-infected patients. Chronic HIV infection sustains an interferon-inducible gene signature with marked upregulation of interferon-stimulated genes such as MxA and ISG15. While acute IFN production is protective, the chronic presence of HIV infection activates several pathological pathways that directly cause muscle inflammation and damage.[38-40] The interaction between the HIV envelope protein gp120 and CD4 receptors on plasmacytoid dendritic cells directly triggers the sustained production of IFN-α.[41] This constant fuelling of the IFN pathway directly maintains the systemic inflammatory state essential for the development of autoimmune manifestations, including myositis.[42] Interferon concentrations during HIV infection markedly up-regulate MHC genes on the sarcolemma fibres that enable constant autoantigen presentation through histocompatibility proteins to the cytotoxic CD8+ T cells. This directly results in recognition and targeted destruction of muscle tissue in susceptible HIV-infected individuals.[43] In the context of dermatomyositis, IFN directly drives vasculopathy by disrupting vascular

networks.[44, 45] Historically, muscle biopsies in HIV patients consistently show tubuloreticular inclusions in endothelial capillary cells, recognised as a hallmark morphological marker of intense IFN signalling.[46] Even after ART initiation and viral load reduction, persistent IFN signalling and ISG upregulation remain in peripheral blood and lymphoid organs; thus, preclinical and clinical evidence prevails in persistent muscle IFN inflammation during HIV infection.[47, 48]

Autoimmunity in HIV may mimic systemic lupus erythematosus (SLE)-like syndromes, vasculitides (including polyarteritis nodosa), antiphospholipid syndrome, and sicca syndrome. Serological evidence of autoantibodies during flares of autoimmunity has been documented (e.g., antinuclear antibodies, anticardiolipin antibodies, and lupus anticoagulant) in the context of persistent immune activation characteristic of chronic HIV infection[8]. The formation and deposition of circulating immune complexes in HIV-infected patients have significant pathological implications, indicating a predisposition to systemic autoimmune conditions, ranging from systemic immune activation to severe end-organ damage.[49] These complexes, which consist of HIV antigens (p24, gp41, and gp160) bound to polyclonal IgG or IgA antibodies, represent one of the earliest detectable B-cell responses to the virus. The circulating complexes participate in the activation of immune cells and the complement system. Patients with AIDS often bear C3bi fragments, suggesting they trigger the alternative complement pathway rather than the classical pathway. This continuous activation contributes to an inflammatory intravascular milieu that leads to non-AIDS comorbidities such as accelerated organ ageing and damage.[50-52] The dynamic interplay of bacterial and viral antigens and host antibody response changes throughout the course of HIV-1 infection. Initial HIV immune responses potentially lack protective efficacy due to non-selective of virions.[50] The ongoing formation of these early immune complexes is recognised as a significant contributor to systemic immune activation and lupus-like activity and disease progression.[53] This process is further complicated in opportunistic infections, which exacerbate immune antibody formation and immune complex deposition with tissue inflammation, potentially contributing to persistent lupus-like manifestations.[34]

Sicca syndrome occurring in the context of HIV infection is multifactorial. HIV infection may manifest with symptoms resembling Sjögren's syndrome, potentially due to chronic immunoactivation. The interaction between early and chronic immune activation and genetic predisposition, possibly initiated by environmental factors, may contribute to the development of de novo exocrine gland autoantibodies.[54] HIV-infected individuals may exhibit clinical manifestations of sicca symptoms and focal lymphocytic sialoadenitis, resembling Sjögren's syndrome, but critical immunopathological features, including the presence of Ro/La autoantibodies, are frequently lacking.[55] This difference in autoantibody profiles points to different underlying pathogenic mechanisms and the specific immunological pathways that are involved in HIV-associated sicca manifestations as opposed to classical Sjögren's syndrome.[56] For instance, diffuse infiltrative lymphocytosis syndrome (DILS) in HIV-infected patients presents with sicca symptoms and parotid gland enlargement similar to Sjögren's syndrome. DILS is fundamentally characterised by an oligoclonal expansion of CD8+ T cells in response to HIV antigens, infiltrating the salivary and lacrimal glands.[57] This condition has a prevalence of approximately 3% of HIV-positive patients, and it differs significantly from primary Sjögren's syndrome. A greater degree of salivary gland enlargement and extraglandular concomitant disease, such as lymphoid interstitial pneumonitis, with the absence of anti-Ro/La and rheumatoid factor and a great reduction in incidence with highly active antiretroviral therapy, distinguish DILS from Sjögren syndrome.[58, 59]

Dermatologic and vasculitides within the spectrum of HIV-associated immune dysregulation

The ongoing immune dysregulation during HIV has an imbalance in cooperative cells like Th1/Th2 and Th17/Treg homeostasis, creating a permissive environment for the development and exacerbation of various autoimmune dermatological components. The presence of HIV can also profoundly influence Langerhans cells and T regulatory cells, further compromising immunological self-tolerance and potentially exacerbating autoimmune responses in the skin. The specific mechanisms underpinning this dysregulation include alterations in cytokine profiles and diminished lymphoid populations, which together foster an environment conducive to exaggerated inflammation and hypersensitivity within cutaneous tissues.[60, 61]

Psoriasis is notably exacerbated in advanced HIV, despite low CD4 counts. This immune-mediated skin inflammation occurs with increased frequency, with an incidence ratio of 2.05. This is paradoxical because psoriasis is a T-cell-mediated disease, and immunosuppression would be expected to ameliorate it.[62] The pathogenesis involves CD8 T-cell expansion and superantigen-mediated polyclonal T-cell activation from HIV proteins and self-antigens.[63] Also, other non-adaptive T cells play a role in psoriasis pathogenesis that may overcome the immune deficit of CD4+ T cell depletion. Particularly CD4- and/or CD8- (double-negative) T cells contribute to the psoriasis cytokine burden, such as γδ T cells playing a great immunopathogenic role.[64] Psoriasis typically involves Vγ9Vδ2 T cells in resolving acute inflammation; their chronic dysfunction or absence in HIV patients treated with ART may contribute to increased severity or duration of psoriatic lesions.[65] HIV patients may experience particularly severe and persistent skin lesions, including guttate, inverse, and erythrodermic subtypes, which are more aggressive than those typical in HIV-negative individuals. HIV-associated psoriasis poses unique management challenges because conventional systemic treatments might be contraindicated or require dose adjustments to mitigate toxicity; further research into novel biological therapies with concerns about altered immune function might initially hinder their use.[66, 67]

Other severe noninfectious inflammatory and hypersensitivity skin conditions are also common. Several other noninfectious inflammatory and hypersensitivity-

related skin conditions are prevalent in HIV patients, often presenting with increased severity, such as keratoderma blennorrhagicum, a psoriasiform skin rash that often presents extensively; and atopic dermatitis-like eruptions, particularly in HIV-infected paediatric cases and those with a family history of atopy.[61, 68] A paradoxical autoimmune blistering disorder reported in HIV-infected individuals is bullous pemphigoid, sometimes presenting alongside other autoimmune manifestations.[69] The prevalence of such disorders has generally increased with the restoration of T-cell immunity facilitated by antiretroviral therapy in patients living with an HIV infection and frequently exhibiting specific inflammatory skin markers.[70]

Direct vascular injury from HIV replication or opportunistic pathogens, chronic immune activation, and molecular mimicry between HIV proteins and self-antigens contribute to the pathogenesis of HIV-associated vasculitis. Recruited inflammatory cells release reactive oxygen species, metalloproteinases, and cytokines, inducing direct endothelial injury and apoptosis, which is exacerbated by HIV replication. Vessel wall necrosis and a prothrombotic state characterise vasculitic endothelial damage.[71, 72] Moreover, uncontrolled HIV infection is associated with elevated inflammatory markers, such as C-reactive protein, that contribute to vascular inflammatory pathogenesis.[73]

The immune system activation is linked to vasculitis via the formation and deposition of circulating immune complexes containing HIV antigens with an IgG or IgA isotype along the vascular endothelium. Immune complex composition within the vessel wall is dynamic. During early infection, these complexes nonselectively bind to HIV virions, potentially impairing the host's initial neutralising antibody response. Such early antibodies promote endothelial damage alongside oligoclonal B-cell expansion.[47, 74] Late complex deposition activates complement, often via the alternative pathway, as evidenced by excessive circulating C3bi fragments in HIV-infected patients.[75] Complexes bind to Fc receptors, generating anaphylatoxins (C3a/C5a) that promote endothelial activation, increased vascular permeability, and chemotaxis of neutrophils and monocytes.[76] Immune complexes underlie various autoimmune-like manifestations in HIV-associated vasculitides, including polyarteritis nodosa-like presentations.[77] Serum cryoglobulins and anti-neutrophil cytoplasmic antibodies, particularly perinuclear ANCA (pANCA), are also common in HIV-infected individuals, although their role in ANCA-associated vasculitis pathogenesis remains unclear.[78] Many HIV-associated vasculitides show nonspecific neutrophilic or monocytic vascular inflammation with heterogeneous clinical features, including cutaneous rash and peripheral neuropathy, complicating classification.[79] There are no specific vascular-size complications during HIV immune vasculitic flares. Large-vessel involvement, such as aortoiliac vasculopathy, often features fibroproliferative granulomatous inflammation and false aneurysm formation,[80] whereas small-vessel vasculitis manifests with features like mixed cryoglobulinaemia and neurological symptoms, particularly in patients with CD4 counts <300 cells/μL.[81, 82] Further complexity arises in HIV-associated vasculitis, with unforeseen complications of affected vessels, with conditions like Takayasu arteritis, Henoch-Schonlein purpura, Behçet-like endothelial damage and central nervous system (CNS) vasculitis still being prevalent in the HIV-positive population.[83, 84]

Haematologic autoimmune manifestations in HIV infection

The altered immune environment in HIV infection creates a fertile ground for both haematologic autoimmunity and the development of haematological neoplasms like lymphoma. This is driven by a complex interplay of chronic immune activation, loss of surveillance, and genetic instability within the B-cell compartment. Haematologic autoimmune conditions are among the most prevalent inflammatory and autoimmune manifestations in people living with HIV. Conditions such as immune thrombocytopenia (ITP), autoimmune haemolytic anaemia (AIHA), and autoimmune neutropenia are frequently observed in HIV-induced immune dysregulation of haematological systems.[85, 86]

Autoimmune cytopenias, such as autoimmune haemolytic anaemia and immune thrombocytopenia seen in HIV, reflect dysregulated B-cell activity and autoantibody production. HIV triggers the expansion of polyclonal and polyreactive B cells, which leads to the overproduction of autoantibodies against host blood antigens. There is also evidence of molecular mimicry between specific HIV proteins and self-antigens, which may cross-react and initiate systemic autoimmune responses.[87, 88, 89] These haematologic manifestations are often associated with profound immune system perturbations, including chronic immune activation, altered cytokine profiles, and a loss of immune tolerance, leading to the destruction of healthy blood cells by the body's own immune system.[90] Large cohort studies have shown a significantly higher prevalence of AIHA among HIV-infected individuals compared to matched controls.[91, 92]

Immune thrombocytopenia is the most frequently reported autoimmune condition in HIV patients, with a dramatically elevated risk (adjusted hazard ratio 8.34) compared to the general population. The global prevalence of thrombocytopenia among HIV-infected adults is approximately 17.9%. Processes such as heightened antiplatelet antibody production are significant contributors to morbidity in HIV-positive patients.[93] HIV-associated immune thrombocytopenia is notable for increased platelet-associated IgG and complement components C3 and C4, distinguishing it from classic autoimmune thrombocytopenic purpura. This condition is further compounded by cross-reacting antibodies targeting viral glycoproteins, which can inadvertently bind to platelet membrane surface glycoproteins, leading to their destruction.[94] Bone marrow suppression may also arise with HIV infection, causing selective thrombocytopenia, which is added to the exacerbated immune-mediated platelet destruction.[95] Severe thrombocytopenia may also manifest in the context of ART reconstitution and HIV-associated secondary thrombotic thrombocytopenic purpura, with high C5 complement activation and anti-

ADAMTS13 circulating autoantibodies, highlighting the multifaceted haematological complications of HIV infection.[96, 97]

Specific antineutrophil autoantibodies, observed in a significant proportion of HIV-infected individuals, are highly correlated with the development of neutropenia by immune-mediated neutrophil destruction caused by antibodies targeting neutrophil cytoplasmic molecules such as myeloperoxidase and elastase.[98, 99] HIV infection itself can directly suppress bone marrow function, leading to decreased haematopoiesis, granulopoiesis, and subsequent cytopenias.[100]

The immune dysregulation in HIV also leads to B-cell hyperactivation, characterised by elevated serum immunoglobulins and autoantibodies, contributing to increased incidence of B-cell neoplasms and impaired humoral responses.[101] The transformation of the immune system into a pro-oncogenic state is a multi-step process involving both indirect and direct viral mechanisms that explains the pathogenesis of haematological neoplasms.[102, 103] The transition from autoimmunity to neoplasm in HIV is largely mediated by a B-cell compartment that is simultaneously overstimulated and under-regulated by inflammation due to T-cell deficiency that tries to contain infections of EBV, HPV, HBV and HCV, Kaposi's sarcoma or other oncogenic viral infections.[104, 105]

Secondary haemophagocytic lymphohistiocytosis in the context of HIV infection

Secondary HLH is a rare but serious complication in patients with HIV. Most patients with HLH and HIV are substantially immunosuppressed, with more than 80% having CD4 counts <200 cells/µL. In approximately 70% of cases, HLH may be triggered by opportunistic or non-opportunistic infections, malignancies, or the initiation of highly active antiretroviral therapy, while about 30% have no apparent trigger.[106] HLH-2004 and the HScore criteria establish that the CD4+ depletion due to HIV infection is a major feature of HLH triggers. Lymphomas and HHV-8-associated diseases are particularly common triggers in people living with HIV. In a recent cohort, 20 of 22 patients (91%) with HLH had a lymphoproliferative disorder as a trigger, including Hodgkin lymphoma (36%), HHV-8-positive multicentric Castleman disease (23%), and HHV-8-positive primary effusion lymphoma (14%).[107]

The pathophysiology of haemophagocytic syndrome in HIV patients is multifactorial and follows the threshold model, where the underlying immunosuppression caused by HIV combines with background inflammation, opportunistic infectious triggers, and possible genetic susceptibility until a critical threshold is reached that triggers uncontrolled hyperinflammation. The central defect in HLH is an alteration in granule-mediated cytotoxicity, a mechanism that follows perforin and Fas-FasL systems activation and macrophage overstimulation through antigen presentation and proinflammatory cytokine production.[108] The inability of NK cells and CD8+ T cells to lyse infected or activated antigen-presenting cells results in prolonged cell-cell interactions with amplification of a pro-inflammatory cytokine cascade. An exaggerated inflammatory response caused by the hypersecretion of proinflammatory cytokines, including interferon-γ, tumour necrosis factor-alpha (TNF-α), and interleukin (IL)-6, IL-8, IL-12, IL-21, IL-27, IL-1β and IL-18, is known as a “cytokine storm" that is pathogenically linked to the development of the main clinical and laboratory features of HLH and contributes to tissue damage and progressive systemic organ failure.[109] These mechanisms fail in overcoming the initial noxious signal, entering a vicious cycle of increased antigen presentation and repeated interferon-γ-dependent stimulation of danger-associated molecule receptors, causing uncontrolled activation of new antigen-presenting cells and recruitment of potentially life-threatening macrophages and myeloid cells, primarily through interferon-γ (IFN-γ). Hyperactivated macrophages are the final effectors of systemic organ damage by infiltrating the liver, spleen and bone marrow and even the CNS, perpetuating inflammation with uncontrolled phagocytosis that depletes erythrocytes, leukocytes and thrombocytes within.[110]

HIV by itself can act as an acute trigger during primary HIV infection. Cases of HLH have been reported as a manifestation of acute HIV infection, with extremely high plasma viral loads (>10,000,000 copies/mL).[111] More than 80% of patients with HLH and HIV are substantially immunosuppressed, with CD4+ counts <200 cells/µL. Elevated ferritin in HIV reflects both the acute-phase response and dysregulated iron metabolism, and extreme hyperferritinemia may signal life-threatening conditions. Ferritin concentrations in HIV-infected patients increase with clinical worsening of infection and with decreasing CD4+ lymphocyte counts.[112] This chronic immunosuppression creates a state of vulnerability that facilitates the surge of HLH with additional triggers such as opportunistic infections, including *Mycobacterium spp.* (34%), Cytomegalovirus (14%), *Cryptococcus neoformans* (11%), Epstein-Barr virus (26%), and *Histoplasma capsulatum* (17%).[113]

Finally, a study of 80 HIV patients with advanced disease (CD4 <100 cells/µL) and mycobacterial infections found that severe IRIS can have features overlapping with HLH [6]. Patients meeting HLH criteria while initiating ART have adopted the term "HLH-IRIS" or "hyperferritinemic IRIS". Patients developing HLH-IRIS required corticosteroids more frequently (OR 21.5) and longer hospitalisation days. Ferritin, CXCL9, and soluble CD25 are useful diagnostic markers for HLH at IRIS onset, while haemoglobin <9.2 g/dL is a pre-ART predictor of HLH-IRIS.[114]

Central Nervous System Autoimmunity within HIV infection

Neurological manifestations of the central nervous system (CNS) mediated by autoimmunity in patients with HIV infection include demyelinating disorders, autoimmune encephalitis, and inflammatory syndromes related to immune reconstitution inflammatory syndromes. A recent study identified that people living with HIV can present with acute neurological symptoms and positive anti-CNS

antibodies. In this series of 12 patients, inflammatory features were observed in the cerebrospinal fluid (CSF) with non-specific anti-CNS antibodies in all subjects and a specific antibody in one of them (recoverine and Zic4). Magnetic resonance imaging showed demyelinating lesions, inflammatory lesions, or no lesions.[115]

Cases of anti-NMDA receptor antibody-mediated encephalitis have been reported in patients with HIV. These cases can present with encephalopathy, seizures, and cognitive impairment, particularly in the context of "HIV escape into the CSF" (discordant increase in CSF viral load[115]). One notable case described limbic encephalitis associated with anti-NMDA antibodies in a patient with primary HIV infection and Kaposi's sarcoma.[116] Demyelinating disorders resembling multiple sclerosis (MS) and neuromyelitis optica (NMO) have also been described in HIV-positive patients. One case reported a patient with mixed features of NMO and MS, with longitudinally extensive transverse myelitis in the thorax and oligoclonal bands in the CSF, but without the presence of anti-aquaporin 4 antibodies.[117] HIV-associated demyelinating leukoencephalopathy is characterised by massive CNS infiltration by HIV-infected monocytes and macrophages and extensive white matter destruction, particularly in patients who fail antiretroviral therapy (ART). Vacuolar myelopathy, although not strictly autoimmune, exhibits demyelination characteristics with intralamellar vacuolation in the spinal white matter.[118]

Alarmins such as IL-33 and HMGB1 contribute to HIV-induced neuropathogenesis, with neurocognitive alterations associated with dysregulation of the IL-33/ST2 axis in the CNS. This adds to the hypothesis of neuropsychiatric immune-mediated manifestations of HIV patients initiating ART.[119] Similarly, IRIS represents an immunopathological response resulting from the rapid restoration of specific immune responses against pre-existing antigens combined with immune dysregulation, occurring shortly after the initiation of antiretroviral therapy.[120] CNS IRIS is characterised by an intense inflammatory reaction to dead or dormant organisms, or to autoantigens, due to an increased but dysregulated immune response. The infiltration of CD8+ cells into the leptomeninges, perivascular spaces, blood vessels, and even parenchyma appears to be the pathological hallmark of CNS-IRIS.[121] IRIS associated with progressive multifocal leukoencephalopathy (PML) can present with acute neurological deterioration and contrast-enhancing demyelinating lesions, even if immunological and virological measures show improvement in HIV status. The pathogenesis of these autoimmune manifestations involves several mechanisms. HIV induces cytokines such as IL-1β, TNF-α, and IL-6, which can lead to an autocrine feedback loop involving increased productive viral replication and induction of other neural cytokines. Viral proteins circulating in the blood can induce cerebral endothelial cells to release cytokines, invoking another source of neuroinflammation.[121, 122]

Conclusion

HIV infection creates a milieu of chronic immune activation, regulatory T-cell failure, and polyclonal B-cell/molecular mimicry–driven autoantibody production. Clinically, this yields a wide range of autoimmune-like syndromes often amplified or unmasked during immune reconstitution on ART. Current guidelines do not recommend routine autoantibody screening for asymptomatic HIV-positive patients on ART. The presence of autoantibodies does not necessarily indicate autoimmune disease, as they often reflect polyclonal B-cell activation. Instead, monitoring strategies focus on clinical surveillance, standard laboratory monitoring for ART safety and efficacy, and symptom-directed evaluation when autoimmune manifestations are suspected. High-risk periods for autoimmune manifestations include the first 3-9 months after ART initiation for IRIS-related autoimmunity and during long-term therapy with good immunologic control with suspected organ dysfunction due to residual inflammation. Patients should be monitored closely during the first weeks to months after treatment initiation for new or worsening inflammatory symptoms, including fever, lymphadenopathy, worsening pulmonary infiltrates, or new organ-specific autoimmune symptoms.

In summary, HIV infection is associated with a wide and paradoxical array of autoimmune manifestations affecting multiple organ systems, driven by complex immune dysregulation and sometimes exacerbated by immune reconstitution. Many treatments directed towards regulating autoimmunity in this population raise concerns in clinicians – if the ongoing immune deficiency by HIV, with or without ART, should be further manipulated by these modulatory targets, careful evaluation must be sought in every case.

Conflicts of Interest Statement

The authors declare no conflict of interest of any kind during the process of writing this literature review.

References

1. Lederman MM, Funderburg NT, Sekaly RP, Klatt NR, Hunt PW. Residual Immune Dysregulation Syndrome in Treated HIV infection. In: Advances in Immunology. Vol 119. Elsevier; 2013:51-83. doi:10.1016/B978-0-12-407707-2.00002-3
2. Meng Z, Du L, Hu N, et al. Antiretroviral Therapy Normalizes Autoantibody Profile of HIV Patients by Decreasing CD33+CD11b+HLA-DR+ Cells. Medicine. 2016;95(15):e3285. doi:10.1097/MD.0000000000003285
3. Korolevskaya LB, Shmagel KV, Shmagel NG. Characteristics of Circulating Immune Complexes in HIV-Infected Patients with Different Viral Load. Bulletin of Experimental Biology and Medicine. 2015;159(4):469-471. doi:10.1007/s10517-015-2994-6
4. Wilson EMP, Sereti I. Immune restoration after antiretroviral therapy: the pitfalls of hasty or incomplete repairs. Immunological Reviews. 2013;254(1):343-354. doi:10.1111/imr.12064
5. Hajhamed NM, Mohammed SI, Hussein WA, et al. Mapping of the Antinuclear Autoantibodies in Sudanese patients infected with Human Immunodeficiency Virus after HAART receiving: A cross-sectional study. Scientific Reports. 2025;15(1):23367. doi:10.1038/s41598-025-06389-9
6. Poizot-Martin I, Rosenthal E, Gilbert C, et al. Nadir CD4 Is Negatively Associated With Antinuclear Antibody Detection in HCV/HIV-Coinfected Patients. JAIDS Journal of Acquired Immune Deficiency Syndromes. 2019;80(4):461-466. doi:10.1097/QAI.0000000000001940
7. Bekker LG, Beyrer C, Mgodi N, et al. HIV infection. Nature Reviews Disease Primers. 2023;9(1):42. doi:10.1038/s41572-023-00452-3
8. Gunawan CK, Sumarpo A, Indrati AR. Immune Dysregulation in HIV-TB Co-Infection: Role of Cytokines and T Cell Biomarkers—A Narrative Review. Pathogens. 2026;15(1):51. doi:10.3390/pathogens15010051
9. Longenecker CT, Sullivan C, Baker JV. Immune activation and cardiovascular disease in chronic HIV infection. Current Opinion in HIV and AIDS. 2016;11(2):216-225. doi:10.1097/COH.0000000000000227
10. Twigg HL, Crystal R, Currier J, et al. Refining Current Scientific Priorities and Identifying New Scientific Gaps in HIV-Related Heart, Lung, Blood, and Sleep Research. AIDS Research and Human Retroviruses. 2017;33(9):889-897. doi:10.1089/aid.2017.0026
11. Kardava L, Moir S. B-cell abnormalities in HIV-1 infection. Current Opinion in HIV and AIDS. 2019;14(4):240-245. doi:10.1097/COH.0000000000000547
12. Collins DR, Gaiha GD, Walker BD. CD8+ T cells in HIV control, cure and prevention. Nature Reviews Immunology. 2020;20(8):471-482. doi:10.1038/s41577-020-0274-9
13. Kazer SW, Walker BD, Shalek AK. Evolution and Diversity of Immune Responses during Acute HIV Infection. Immunity. 2020;53(5):908-924. doi:10.1016/j.immuni.2020.10.015
14. Vega LE, Espinoza LR. Human immunodeficiency virus infection (HIV)–associated rheumatic manifestations in the pre- and post-HAART eras. Clinical Rheumatology. 2020;39(9):2515-2522. doi:10.1007/s10067-020-05082-8
15. Silveira LH, Jara LJ, Martínez-Osuna P, Espinoza LR, Seleznick MJ. Musculoskeletal Manifestations of Human Immunodeficiency Virus Infection. Journal of Intensive Care Medicine. 1991;6(3):106-116. doi:10.1177/088506669100600302
16. Iordache L, Launay O, Bouchaud O, et al. Autoimmune diseases in HIV-infected patients: 52 cases and literature review. Autoimmunity Reviews. 2014;13(8):850-857. doi:10.1016/j.autrev.2014.04.005
17. Suleman FE, Ally MMTM. Human immunodeficiency virus infection and inflammatory arthritis: A review of clinical and imaging features. South African Journal of Radiology. 2017;21(2). doi:10.4102/sajr.v21i2.1261
18. Walker UA, Tyndall A, Daikeler T. Rheumatic conditions in human immunodeficiency virus infection. Rheumatology. 2008;47(7):952-959. doi:10.1093/rheumatology/ken132
19. Kibret AK, Yitayal MM, Eriku GA, Gashaw M, Yalew ES, Weldetsadik FK. Self-reported musculoskeletal disorders and associated factors among HIV/AIDS patients following ART at University of Gondar Comprehensive Specialized Hospital, Gondar, Ethiopia, 2021: A cross-sectional study design. BMC Infectious Diseases. 2023;23(1):540. doi:10.1186/s12879-023-08497-1
20. Zalavras CG, Dellamaggiora R, Patzakis MJ, Bava E, Holtom PD. Septic Arthritis in Patients with Human Immunodeficiency Virus. Clinical Orthopaedics and Related Research. 2006;451:46-49. doi:10.1097/01.blo.0000229305.97888.17
21. Fox C, Walker-Bone K. Evolving spectrum of HIV-associated rheumatic syndromes. Best Practice & Research Clinical Rheumatology. 2015;29(2):244-258. doi:10.1016/j.berh.2015.04.019
22. Cunha BM, Mota LMH, Pileggi GS, Safe IP, Lacerda MVG. HIV/AIDS and rheumatoid arthritis. Autoimmunity Reviews. 2015;14(5):396-400. doi:10.1016/j.autrev.2015.01.001
23. Calabrese LH, Kirchner E, Shrestha R. Rheumatic Complications of Human Immunodeficiency Virus Infection in the Era of Highly Active Antiretroviral Therapy: Emergence of a New Syndrome of Immune Reconstitution and Changing Patterns of Disease. Seminars in Arthritis and Rheumatism. 2005;35(3):166-174. doi:10.1016/j.semarthrit.2005.03.007
24. Toit R du, Whitelaw D, Taljaard JJ, Plessis L du, Esser M. Lack of specificity of anticyclic citrullinated peptide antibodies in advanced human immunodeficiency virus infection. The Journal of rheumatology. 2011;38(6):1055-1060. doi:10.3899/jrheum.100713
25. Kim SH, Lee SH. Updates on ankylosing spondylitis: pathogenesis and therapeutic agents. Journal of Rheumatic Diseases. 2023;30(4):220-233. doi:10.4078/jrd.2023.0041

26. Adizie T, Moots RJ, Hodkinson B, French N, Adebajo AO. Inflammatory arthritis in HIV positive patients: A practical guide. BMC Infectious Diseases. 2016;16(1):100. doi:10.1186/s12879-016-1389-2
27. Hunt PW. Th17, gut, and HIV: therapeutic implications. Current Opinion in HIV and AIDS. 2010;5(2):189-193. doi:10.1097/COH.0b013e32833647d9
28. Marchetti G, Bellistrì GM, Borghi E, et al. Microbial translocation is associated with sustained failure in CD4+ T-cell reconstitution in HIV-infected patients on long-term highly active antiretroviral therapy. AIDS. 2008;22(15):2035-2038. doi:10.1097/QAD.0b013e3283112d29
29. Ouédraogo DD, Ntsiba H, Zabsonré JT, et al. Clinical spectrum of rheumatologic diseases in a department of rheumatology in Ouagadougou (Burkina Faso). Clinical rheumatology. 2014;33(3):385-389. doi:10.1007/s10067-013-2455-4
30. Saigal R, Chakraborty A, Yadav RN, Goyal LK. Rheumatological Manifestations in HIV-Positive Patients: A Single-Center Study. Advances in Therapy. 2020;37(10):4336-4345. doi:10.1007/s12325-020-01470-3
31. Casado E, Olivé A, Holgado S, et al. Musculoskeletal manifestations in patients positive for human immunodeficiency virus: correlation with CD4 count. The Journal of rheumatology. 2001;28(4):802-804.
32. Njobvu P, McGill P. Psoriatic arthritis and human immunodeficiency virus infection in Zambia. The Journal of rheumatology. 2000;27(7):1699-1702.
33. Miedema F, Hazenberg MD, Tesselaar K, Baarle D van, Boer RJ de, Borghans JAM. Immune Activation and Collateral Damage in AIDS Pathogenesis. Frontiers in Immunology. 2013;4. doi:10.3389/fimmu.2013.00298
34. Sereti I, Altfeld M. Immune activation and HIV. Current Opinion in HIV and AIDS. 2016;11(2):129-130. doi:10.1097/COH.0000000000000244
35. Sheets K, Baker JV. HIV and Inflamm-Aging: How Do We Reach the Summit of Healthy Aging? Topics in antiviral medicine. 2024;32(5):589-596.
36. Mody G. Articular manifestations of human immunodeficiency virus infection. Best Practice & Research Clinical Rheumatology. 2003;17(2):265-287. doi:10.1016/S1521-6942(03)00003-2
37. Lloyd TE, Pinal-Fernandez I, Michelle EH, et al. Overlapping features of polymyositis and inclusion body myositis in HIV-infected patients. Neurology. 2017;88(15):1454-1460. doi:10.1212/WNL.0000000000003821
38. Ding J, Ma L, Zhao J, et al. An integrative genomic analysis of transcriptional profiles identifies characteristic genes and patterns in HIV-infected long-term non-progressors and elite controllers. Journal of Translational Medicine. 2019;17(1):35. doi:10.1186/s12967-019-1777-7
39. Echebli N, Tchitchek N, Dupuy S, et al. Stage-specific IFN-induced and IFN gene expression reveal convergence of type I and type II IFN and highlight their role in both acute and chronic stage of pathogenic SIV infection. PLOS ONE. 2018;13(1): e0190334. doi:10.1371/journal.pone.0190334
40. Plaçais L, Joly C, d'Urbano V, et al. Increased IFN responses drive myeloid cell activation in people living with HIV-1. Scientific Reports. 2025;15(1):20627. doi:10.1038/s41598-025-04613-0
41. Herbeuval JP, Shearer GM. HIV-1 immunopathogenesis: how good interferon turns bad. Clinical immunology (Orlando, Fla). 2007;123(2):121-128. doi:10.1016/j.clim.2006.09.016
42. Fitzgerald-Bocarsly P, Jacobs ES. Plasmacytoid dendritic cells in HIV infection: striking a delicate balance. Journal of Leukocyte Biology. 2010;87(4):609-620. doi:10.1189/jlb.0909635
43. Rayavarapu S, Coley W, Kinder TB, Nagaraju K. Idiopathic inflammatory myopathies: pathogenic mechanisms of muscle weakness. Skeletal Muscle. 2013;3(1):13. doi:10.1186/2044-5040-3-13
44. Baechler EC, Bauer JW, Slattery CA, et al. An Interferon Signature in the Peripheral Blood of Dermatomyositis Patients is Associated with Disease Activity. Molecular Medicine. 2007;13(1-2):59-68. doi:10.2119/2006-00085.Baechler
45. Greenberg SA. Dermatomyositis and Type 1 Interferons. Current Rheumatology Reports. 2010;12(3):198-203. doi:10.1007/s11926-010-0101-6
46. Nelke C, Kleefeld F, Preusse C, Ruck T, Stenzel W. Inclusion body myositis and associated diseases: an argument for shared immune pathologies. Acta Neuropathologica Communications. 2022;10(1):84. doi:10.1186/s40478-022-01389-6
47. Han R, Yu H, Li G, Su L, Cheng L. Persistent Type I Interferon Signaling Impairs Innate Lymphoid Cells During HIV-1 Infection Under Suppressive ART. Viruses. 2025;17(8):1099. doi:10.3390/v17081099
48. Su L. Pathogenic Role of Type I Interferons in HIV-Induced Immune Impairments in Humanized Mice. Current HIV/AIDS Reports. 2019;16(3):224-229. doi:10.1007/s11904-019-00444-7
49. Korolevskaya LB, Shmagel KV, Shmagel NG, Saidakova EV. Systemic activation of the immune system in HIV infection: The role of the immune complexes (hypothesis). Medical Hypotheses. 2016;88:53-56. doi:10.1016/j.mehy.2016.01.009
50. Liu P, Overman RG, Yates NL, et al. Dynamic Antibody Specificities and Virion Concentrations in Circulating Immune Complexes in Acute to Chronic HIV-1 Infection. Journal of Virology. 2011;85(21):11196-11207. doi:10.1128/JVI.05601-11
51. Tausk FA, McCutchan A, Spechko P, Schreiber RD, Gigli I. Altered erythrocyte C3b receptor expression, immune complexes, and complement activation in homosexual men in varying risk groups for acquired immune deficiency syndrome. Journal of Clinical Investigation. 1986;78(4):977-982. doi:10.1172/JCI112688
52. Alcaide ML, Parmigiani A, Pallikkuth S, et al. Immune Activation in HIV-Infected Aging Women on Antiretrovirals—Implications for Age-Associated Comorbidities: A Cross-Sectional Pilot Study. PLoS ONE. 2013;8(5):e63804. doi:10.1371/journal.pone.0063804
53. Pastushenkov V, Mitin Y, Semenov A, Valutite D, Dudnikov S, Gabaeva M. Medical-biological significance of specific CIC and good perspectives of immune complex disintegration using ultrasonic in

laboratory diagnostics of HIV-infection. Vestnik of Saint Petersburg University Medicine. 2020;15(4):239-245. doi:10.21638/spbu11.2020.402
54. Zhang SX, Fan CH, Jing ZN, et al. Genetic Evidence Supporting Causal Associations Between Viral Infections and Sjogren's Syndrome. Published online October 2024. doi:10.21203/rs.3.rs-5006632/v1
55. Vitali C. Immunopathologic differences of Sjögren's syndrome versus sicca syndrome in HCV and HIV infection. Arthritis Research & Therapy. 2011;13(4):233. doi:10.1186/ar3361
56. Igoe A, Scofield RH. Autoimmunity and infection in Sjögren's syndrome. Current Opinion in Rheumatology. 2013;25(4):480-487. doi:10.1097/BOR.0b013e32836200d2
57. Itescu S, Winchester R. Diffuse infiltrative lymphocytosis syndrome: a disorder occurring in human immunodeficiency virus-1 infection that may present as a sicca syndrome. Rheumatic diseases clinics of North America. 1992;18(3):683-697.
58. Kazi S, Cohen PR, Williams F, Schempp R, Reveille JD. The diffuse infiltrative lymphocytosis syndrome. Clinical and immunogenetic features in 35 patients. AIDS (London, England). 1996;10(4):385-391.
59. Basu D, Williams FM, Ahn CW, Reveille JD. Changing spectrum of the diffuse infiltrative lymphocytosis syndrome. Arthritis Care & Research. 2006;55(3): 466-472. doi:10.1002/art.21980
60. Isaacs T, Lehloenya R. HIV-associated photodermatitis in African populations. Frontiers in Allergy. 2023;4. doi:10.3389/falgy.2023.1159387
61. Chimbetete T, Buck C, Choshi P, et al. HIV-Associated Immune Dysregulation in the Skin: A Crucible for Exaggerated Inflammation and Hypersensitivity. Journal of Investigative Dermatology. 2023;143(3):362-373. doi:10.1016/j.jid.2022.07.035
62. Touzeau-Roemer V, Skoll M, Tajpara P, et al. Prevalence of Skin-specific Autoantibodies in HIV-infected Patients and Uninfected Controls. Acta Dermato Venereologica. 2019;99(11):978-983. doi:10.2340/00015555-3251
63. Patel RV, Weinberg JM. Psoriasis in the patient with human immunodeficiency virus, part 1: review of pathogenesis. Cutis. 2008;82(2):117-122.
64. Bernal-Alferes B, Gómez-Mosqueira R, Ortega-Tapia GT, et al. The role of γδ T cells in the immunopathogenesis of inflammatory diseases: from basic biology to therapeutic targeting. J Leukoc Biol. 2023;(April):1-14. doi:10.1093/jleuko/qiad046.
65. Pauza CD, Poonia B, Li H, Cairo C, Chaudhry S. γδ T Cells in HIV Disease: Past, Present, and Future. Frontiers in Immunology. 2015;5. doi:10.3389/fimmu.2014.00687
66. Morar N, Willis-Owen SA, Maurer T, Bunker CB. HIV-associated psoriasis: pathogenesis, clinical features, and management. The Lancet Infectious Diseases. 2010;10(7):470-478. doi:10.1016/S1473-3099(10)70101-8
67. Papp KA, Beecker J, Cooper C, et al. Use of Systemic Therapies for Treatment of Psoriasis in People Living with Controlled HIV: Inference-Based Guidance from a Multidisciplinary Expert Panel. Dermatology and Therapy. 2022;12(5):1073-1089. doi:10.1007/s13555-022-00722-0
68. Jakubowska W, Ślusarczyk D, Pisera P, et al. Skin and mucosal lesions in the course of HIV infection. Journal of Education, Health and Sport. 2024;51:37-49. doi:10.12775/JEHS.2024.51.003
69. Foerster Y, Sollfrank L, Rechtien L, Harrer T, Berking C, Sticherling M. Case report: Bullous pemphigoid in HIV-1-positive patients: interplay or coincidence? A case series and review of the literature. Frontiers in Immunology. 2023;14. doi:10.3389/fimmu.2023.1179294
70. Aouam A, Bougossa R, Abroug N, Soua Y, Chakroun M. HIV-associated autoimmune blistering and connective tissue disorders: a case report. HIV & AIDS Review. 2023;22(4):356-359. doi:10.5114/hivar.2023.133176
71. Gherardi R, Belec L, Mhiri C, et al. The spectrum of vasculitis in human immunodeficiency virus–infected patients. a clinicopathologic evaluation. Arthritis & Rheumatism. 1993;36(8):1164-1174. doi:10.1002/art.1780360818
72. Wang T, Green LA, Gupta SK, et al. Transfer of Intracellular HIV Nef to Endothelium Causes Endothelial Dysfunction. PLoS ONE. 2014;9(3): e91063. doi:10.1371/journal.pone.0091063
73. Triant VA, Meigs JB, Grinspoon SK. Association of C-Reactive Protein and HIV Infection With Acute Myocardial Infarction. JAIDS Journal of Acquired Immune Deficiency Syndromes. 2009;51(3):268-273. doi:10.1097/QAI.0b013e3181a9992c
74. Georgy A. Natural Catalytic Antibodies in Norm and in HIV-Infected Patients. In: Understanding HIV/AIDS Management and Care - Pandemic Approaches in the 21st Century. InTech; 2011. doi:10.5772/22294.
75. Dierich MP, Stoiber H. Complement supports progression of HIV and turns neutralising antibodies at low concentration into infection enhancing antibodies. Retrovirology. 2006;3(S1):S90. doi:10.1186/1742-4690-3-S1-S90
76. Mazzuti L, Turriziani O, Mezzaroma I. The Many Faces of Immune Activation in HIV-1 Infection: A Multifactorial Interconnection. Biomedicines. 2023;11(1):159. doi:10.3390/biomedicines11010159
77. Gajera A, Kais S. HIV polyarteritis nodosa-like vasculitis presenting as chronic abdominal pain. Clin Rheumatol. 2009;28:869-872. doi:10.1007/s10067-009-1170-7.
78. Vornicu A, Obrișcă B, Sorohan B, Berechet A, Ismail G. ANCA-associated vasculitis in a HIV-infected patient: a case-based review. BMC Nephrology. 2023;24(1):210. doi:10.1186/s12882-023-03244-9
79. Vega LE, Espinoza LR. Vasculitides in HIV Infection. Current Rheumatology Reports. 2020;22(10):60. doi:10.1007/s11926-020-00945-0
80. Rosenberg A, Bailey P, Rigamer M, Levy M. HIV-Associated Aortitis Causing Rapid Development of an Abdominal Aortic Aneurysm. Annals of Vascular Surgery. 2020;66:669.e11-669.e15. doi:10.1016/j.avsg.2020.01.088
81. Bonnet F, Pineau JJ, Taupin JL, et al. Prevalence of cryoglobulinemia and serological markers of

autoimmunity in human immunodeficiency virus infected individuals: a cross-sectional study of 97 patients. The Journal of rheumatology. 2003;30(9):2005-2010.
82. Cohen P, Roulot D, Ferrière F, et al. Prevalence of cryoglobulins and hepatitis C virus infection in HIV-infected patients. Clinical and experimental rheumatology. 1997;15(5):523-527.
83. Sugimoto T, Tsuda A, Kito K, et al. Henoch-Schönlein purpura in a patient with human immunodeficiency virus infection. Rheumatol Int. 2008;28:615-616. doi:10.1007/s00296-007-0492-5.
84. Roscoe C, Kinney R, Gilles R, Blue S. Behçet's disease diagnosed after acute HIV infection: viral replication activating underlying autoimmunity? International Journal of STD & AIDS. 2015;26(6):432-435. doi:10.1177/0956462414539667
85. Vishnu P, Aboulafia DM. Haematological manifestations of human immune deficiency virus infection. British Journal of Haematology. 2015;171(5):695-709. doi:10.1111/bjh.13783
86. Opie J, Verburgh E, Bailly J, Mayne E, Louw V. Hematological Complications of Human Immunodeficiency Virus (HIV) Infection: An Update From an HIV-Endemic Setting. Open Forum Infectious Diseases. 2024;11(4). doi:10.1093/ofid/ofae162
87. Saif MW. HIV-Associated Autoimmune Hemolytic Anemia: An Update. AIDS Patient Care and STDs. 2001;15(4):217-224. doi:10.1089/10872910151133783
88. Li Z, Nardi MA, Karpatkin S. Role of molecular mimicry to HIV-1 peptides in HIV-1–related immunologic thrombocytopenia. Blood. 2005;106(2):572-576. doi:10.1182/blood-2005-01-0243
89. Moir S, Fauci AS. Pathogenic mechanisms of B-lymphocyte dysfunction in HIV disease. Journal of Allergy and Clinical Immunology. 2008;122(1):12-19. doi:10.1016/j.jaci.2008.04.034
90. Catalfamo M, Saout CL, Lane HC. The role of cytokines in the pathogenesis and treatment of HIV infection. Cytokine & Growth Factor Reviews. 2012;23(4-5):207-214. doi:10.1016/j.cytogfr.2012.05.007
91. Adewumi Aa, Titilope Aa, Osamuedemen Va, et al. Prevalence of HIV-related autoimmune haemolytic anaemia in Lagos, Nigeria. Nigerian Medical Journal. 2014;55(1):63. doi:10.4103/0300-1652.128175
92. Kebede SS, Yalew A, Yesuf T, Melku M, Bambo GM, Woldu B. The magnitude and associated factors of immune hemolytic anemia among human immuno deficiency virus infected adults attending University of Gondar comprehensive specialized hospital north west Ethiopia 2021 GC, cross sectional study design. PLOS ONE. 2022;17(10):e0274464. doi:10.1371/journal.pone.0274464
93. Pate KAM, Mankowski JL. HIV and SIV associated thrombocytopenia: an expanding role for platelets in the pathogenesis of HIV. Drug Discovery Today: Disease Mechanisms. 2011;8(1-2):e25-e32. doi:10.1016/j.ddmec.2011.10.001
94. Pascutti MF, Erkelens MN, Nolte MA. Impact of Viral Infections on Hematopoiesis: From Beneficial to Detrimental Effects on Bone Marrow Output. Frontiers in Immunology. 2016;7. doi:10.3389/fimmu.2016.00364
95. Louw S, Gounden R, Mayne ES. Thrombotic thrombocytopenic purpura (TTP)-like syndrome in the HIV era. Thrombosis Journal. 2018;16(1):35. doi:10.1186/s12959-018-0189-x
96. Rao S, Liparoti A, Giannotta JA, et al. Acquired thrombotic thrombocytopenic purpura and HIV infection: a case report and review of the literature. Annals of Hematology. 2026;105(2):37. doi:10.1007/s00277-026-06733-7
97. Shi X, Sims MD, Hanna MM, et al. Neutropenia during HIV Infection: Adverse Consequences and Remedies. International Reviews of Immunology. 2014;33(6):511-536. doi:10.3109/08830185.2014.893301
98. Rubinstein DB, Farrington GK, O'Donnell C, Hartman KR, Wright DG. Autoantibodies to Leukocyte αMβ2 Integrin Glycoproteins in HIV Infection. Clinical Immunology. 1999;90(3):352-359. doi:10.1006/clim.1998.4668
99. Jaresko GS. Etiology of neutropenia in HIV-infected patients. American Journal of Health-System Pharmacy. 1999;56(suppl_5):S5-S8. doi:10.1093/ajhp/56.suppl_5.S5
100. Dolcetti R, Vaccher E, Carbone A. Lymphoproliferations in People Living with HIV: Oncogenic Pathways, Diagnostic Challenges, and New Therapeutic Opportunities. Cancers. 2025;17(13):2088. doi:10.3390/cancers17132088
101. Zhang Y, Guo W, Zhan Z, Bai O. Carcinogenic mechanisms of virus-associated lymphoma. Frontiers in Immunology. 2024;15. doi:10.3389/fimmu.2024.1361009
102. Silverberg MJ, Neuhaus J, Bower M, et al. Risk of cancers during interrupted antiretroviral therapy in the SMART study. AIDS. 2007;21(14):1957-1963. doi:10.1097/QAD.0b013e3282ed6338
103. Diakite M, Shaw-Saliba K, Lau CY. Malignancy and viral infections in Sub-Saharan Africa: A review. Frontiers in Virology. 2023;3. doi:10.3389/fviro.2023.1103737
104. Borges ÁH, Dubrow R, Silverberg MJ. Factors contributing to risk for cancer among HIV-infected individuals, and evidence that earlier combination antiretroviral therapy will alter this risk. Current Opinion in HIV and AIDS. 2014;9(1):34-40. doi:10.1097/COH.0000000000000025
105. Ramos-Casals M, Brito-Zerón P, López-Guillermo A, Khamashta MA, Bosch X. Adult haemophagocytic syndrome. The Lancet. 2014;383(9927):1503-1516. doi:10.1016/S0140-6736(13)61048-X
106. Henter JI. Hemophagocytic Lymphohistiocytosis. New England Journal of Medicine. 2025;392(6):584-598. doi:10.1056/NEJMra2314005
107. Jordan MB. Hemophagocytic lymphohistiocytosis: A disorder of T cell activation, immune regulation, and distinctive immunopathology. Immunological Reviews. 2024;322(1):339-350. doi:10.1111/imr.13298
108. Crayne CB, Albeituni S, Nichols KE, Cron RQ. The Immunology of Macrophage Activation Syndrome. Frontiers in Immunology. 2019;10. doi:10.3389/fimmu.2019.00119

109. Mukherjee S, Kumar P. The pathophysiology of hemophagocytic lympho-histiocytosis (HLH) syndrome and insights from animal models. Clinical and Experimental Immunology. 2025;219(1). doi:10.1093/cei/uxaf036
110. Manji F, Wilson E, Mahe E, Gill J, Conly J. Acute HIV infection presenting as hemophagocytic lymphohistiocytosis: case report and review of the literature. BMC Infectious Diseases. 2017;17(1):633. doi:10.1186/s12879-017-2732-y
111. Telles JP, Perez M de A, Marcusso R, Correa K, Teixeira RFA, Tobias WM. Hemophagocytic syndrome in patients living with HIV: a retrospective study. Annals of Hematology. 2019;98(1):67-72. doi:10.1007/s00277-018-3500-9
112. Rouphael NG, Talati NJ, Vaughan C, Cunningham K, Moreira R, Gould C. Infections associated with haemophagocytic syndrome. The Lancet Infectious Diseases. 2007;7(12):814-822. doi:10.1016/S1473-3099(07)70290-6
113. Rocco JM, Laidlaw E, Galindo F, et al. Severe Mycobacterial Immune Reconstitution Inflammatory Syndrome (IRIS) in Advanced Human Immunodeficiency Virus (HIV) Has Features of Hemophagocytic Lymphohistiocytosis and Requires Prolonged Immune Suppression. Clinical Infectious Diseases. 2023;76(3):e561-e570. doi:10.1093/cid/ciac717
114. Stroffolini G, Atzori C, Imperiale D, Trunfio M, Perri GD, Calcagno A. Central Nervous System Disorders with Auto-Antibodies in People Living with HIV. Microorganisms. 2024;12(9):1758. doi:10.3390/microorganisms12091758
115. Moloney PB, Hutchinson S, Heskin J, et al. Possible N-methyl-D-aspartate receptor antibody-mediated encephalitis in the setting of HIV cerebrospinal fluid escape. Journal of Neurology. 2020;267(5):1348-1352. doi:10.1007/s00415-019-09693-3
116. Kaddu-Mulindwa D, Roth S, Klees-Rollmann A, Fassbender K, Fousse M. Primary HIV infection presenting with Kaposi sarcoma and limbic encephalitis. Journal of NeuroVirology. 2020;26(2):292-296. doi:10.1007/s13365-019-00815-1
117. Delgado SR, Maldonado J, Rammohan KW. CNS demyelinating disorder with mixed features of neuromyelitis optica and multiple sclerosis in HIV-1 infection. Case report and literature review. Journal of NeuroVirology. 2014;20(5):531-537. doi:10.1007/s13365-014-0260-8
118. McArthur JC, Brew BJ, Nath A. Neurological complications of HIV infection. The Lancet Neurology. 2005;4(9):543-555. doi:10.1016/S1474-4422(05)70165-4
119. Hong S, Banks WA. Role of the immune system in HIV-associated neuroinflammation and neurocognitive implications. Brain, Behavior, and Immunity. 2015;45:1-12. doi:10.1016/j.bbi.2014.10.008
120. Gougeon ML. Alarmins and central nervous system inflammation in HIV-associated neurological disorders. Journal of Internal Medicine. 2017;281(5):433-447. doi:10.1111/joim.12570
121. Post MJD, Thurnher MM, Clifford DB, et al. CNS–Immune Reconstitution Inflammatory Syndrome in the Setting of HIV Infection, Part 1: Overview and Discussion of Progressive Multifocal Leukoencephalopathy–Immune Reconstitution Inflammatory Syndrome and Cryptococcal–Immune Reconstitution Inflammatory Syndrome. American Journal of Neuroradiology. 2013;34(7):1297-1307. doi:10.3174/ajnr.A3183
122. Petito CK. Review of central nervous system pathology in human immunodeficiency virus infection. Annals of Neurology. 1988;23(S1):S54-S57. doi:10.1002/ana.410230715