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INTENSIVE CARE FOR COMPLICATIONS FOLLOWING AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION DURING THE AGRANULOCYTOSIS PERIOD IN PATIENTS WITH AUTOIMMUNE DISEASES

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Abstract. Autologous hematopoietic stem cell transplantation (AHSCT) has become a recognized immunoablative therapy for severe, treatment-refractory autoimmune diseases (ADs), including multiple sclerosis (MS), systemic sclerosis (SSc), and other conditions. The agranulocytosis (profound neutropenia) phase after high-dose conditioning chemotherapy remains the period of highest risk for life-threatening complications, primarily infections and regimen-related toxicities. This expanded narrative review synthesizes current evidence on the incidence, risk factors, diagnosis, and intensive care management of complications during this critical window (typically days 0–14 post-infusion). A comprehensive literature search (PubMed, Scopus, Web of Science, and EBMT guidelines, 2010–2026) identified key data from cohort studies, registries, and expert recommendations. Major complications include febrile neutropenia (>80% incidence), bacterial sepsis (20–40%), invasive fungal infections (5–15% in prolonged neutropenia), engraftment syndrome (10–41% in SSc cohorts), diffuse alveolar hemorrhage, acute kidney injury (up to 30%), and severe mucositis. ICU admission occurs in 8–15% of cases, with leading indications being respiratory failure

and septic shock. Modern supportive strategies—rapid empiric antimicrobials, granulocyte colony-stimulating factor (G-CSF), hemodynamic monitoring, organ support, and multidisciplinary care—have reduced treatment-related mortality during this phase to <2% in experienced centers (compared with historical rates >5–10%). Optimized intensive care protocols, early recognition of complications, and adherence to EBMT recommendations are essential to further improve safety and support broader application of AHSCT in carefully selected AD patients.

Keywords: autologous hematopoietic stem cell transplantation, AHSCT, autoimmune diseases, agranulocytosis, neutropenia, febrile neutropenia, intensive care unit, ICU, engraftment syndrome, infections.

Introduction. Autologous hematopoietic stem cell transplantation (AHSCT) is an established treatment for aggressive, refractory autoimmune diseases (ADs) such as relapsing-remitting or progressive multiple sclerosis (MS) and diffuse cutaneous systemic sclerosis (SSc). The procedure involves mobilization and collection of the patient's own hematopoietic stem cells, followed by high-dose immunosuppressive conditioning (commonly cyclophosphamide 200 mg/kg ± antithymocyte globulin [ATG], or BEAM-like regimens) to eradicate autoreactive immune clones, and subsequent reinfusion of autologous stem cells to rescue hematopoiesis. This "immune reset" promotes long-term remission by allowing reconstitution of a more tolerant immune system (Muraro et al., 2017; Alexander, 2025).

The post-conditioning period is marked by profound pancytopenia, with agranulocytosis (absolute neutrophil count [ANC] $<0.5 \times 10^9$/L) lasting a median of 7–14 days (often 9–12 days depending on conditioning intensity and G-CSF use). During this phase, patients experience severe immunosuppression due to mucosal barrier injury (mucositis), loss of innate immunity, and delayed adaptive recovery. Infectious complications predominate, but non-infectious toxicities—including engraftment syndrome, organ failure, and hemorrhagic events—also contribute significantly to morbidity. Pre-existing organ damage in AD patients (e.g., pulmonary fibrosis or cardiac involvement in SSc, neurological deficits in MS) further amplifies vulnerability.

Although overall treatment-related mortality (TRM) for AHSCT in ADs has declined markedly (from >7% historically to <2–5% in contemporary cohorts), the agranulocytosis phase accounts for the majority of early complications and ICU

admissions (8–15%). Up to 23% of patients experience febrile neutropenia during mobilization alone, and post-infusion ICU needs often stem from sepsis or respiratory compromise (Kalincik et al., 2023; Stephens, 2019).

This narrative review provides a detailed examination of complications and evidence-based intensive care strategies specifically during the neutropenic/agranulocytosis period in adult patients undergoing AHSCT for ADs. It highlights risk stratification, diagnostic approaches, therapeutic interventions, and multidisciplinary management to optimize outcomes.

Methods. This narrative review followed PRISMA-ScR guidelines for scoping and narrative syntheses. Systematic searches were conducted in PubMed, Scopus, Web of Science, Google Scholar, and EBMT resources from January 2010 to April 2026. Search terms included combinations of ("autologous hematopoietic stem cell transplantation" OR "AHSCT" OR "auto-HSCT") AND ("autoimmune diseases" OR "multiple sclerosis" OR "systemic sclerosis") AND ("agranulocytosis" OR "neutropenia" OR "neutropenic phase" OR "febrile neutropenia") AND ("intensive care" OR "ICU" OR "complications" OR "sepsis" OR "infection" OR "engraftment syndrome" OR "supportive care"). Reference lists of key reviews, EBMT guidelines, and registry analyses were hand-searched for additional sources.

Inclusion criteria: English-language peer-reviewed articles, cohort studies, registries, guidelines, or reviews focusing on complications and management in the early neutropenic phase after AHSCT for adult AD patients. Exclusion criteria: pediatric-only studies, allogeneic HSCT-dominant data, case reports without broader context, and pre-2010 publications unless foundational. Approximately 65 sources were screened; 28 high-quality articles, guidelines, and registry reports were included for qualitative synthesis. Data extraction emphasized incidence rates, risk factors, diagnostic tools, ICU interventions, and outcomes. Due to study heterogeneity (varying conditioning regimens, AD subtypes, and center experience), no formal meta-analysis was performed.

Results. Spectrum of Complications During the Agranulocytosis Phase. The agranulocytosis period is dominated by infectious risks secondary to severe neutropenia and chemotherapy-induced mucositis. Febrile neutropenia occurs in over 80% of patients, with documented bacterial bloodstream infections in 20–40% of cases.

Common pathogens include Gram-negative bacilli (*Pseudomonas aeruginosa*, *Klebsiella*, *E. coli*) and Gram-positive organisms. Invasive fungal infections (IFI), primarily candidemia or invasive aspergillosis, develop in 5–15% when neutropenia exceeds 10 days, particularly with high-intensity conditioning or prolonged antibiotic exposure (Park et al., 2006; Stephens, 2019). Viral reactivations (HSV, CMV, EBV) are common but usually controlled with prophylaxis.

Non-infectious complications are also frequent:

- **Severe mucositis** (grade 3–4): 30–50%, leading to severe pain, dysphagia, malnutrition, and requirement for total parenteral nutrition (TPN).
- **Engraftment syndrome (ES)**: Occurs around neutrophil recovery (typically day +8 to +14) in 10–20% of general AD cohorts and up to 41% in SSc patients. Clinical features include non-infectious fever, erythematous rash, non-cardiogenic pulmonary edema, weight gain, and occasionally encephalopathy or multi-organ involvement. Risk factors include older age, cardiac involvement in SSc, and G-CSF use (Strunz et al., 2021; Levin et al., 2022).
- **Pulmonary complications**: Diffuse alveolar hemorrhage (DAH) or idiopathic pneumonia syndrome in <5%, often requiring mechanical ventilation. Pre-existing lung disease in SSc increases risk.
- **Renal and hepatic toxicity**: Acute kidney injury (AKI) in 20–30% (higher with cyclophosphamide), sometimes necessitating renal replacement therapy. Hepatic veno-occlusive disease is rare in autologous settings.
- **Hemorrhagic events**: Thrombocytopenic bleeding or hemorrhagic cystitis.

In AD-specific cohorts, TRM during the neutropenic phase has decreased to <2% in high-volume centers, with overall 100-day TRM around 1–3% (Muraro et al., 2017; Sieiro Santos et al., 2025). However, ICU admission rates remain 8–15%, driven mainly by septic shock and hypoxic respiratory failure.

Intensive Care Management Strategies. Prophylaxis and Monitoring*: Patients are managed in protective isolation (HEPA-filtered rooms) with strict reverse barrier nursing. Standard prophylaxis includes antibacterial (e.g., levofloxacin), antifungal (posaconazole or voriconazole for high-risk cases), and antiviral (acyclovir) agents per EBMT guidelines. Daily clinical assessment, frequent blood cultures during fever, serum*

biomarkers (CRP, procalcitonin, presepsin), galactomannan/β-D-glucan monitoring, and early chest CT for persistent fever (>72–96 hours) are recommended (Dubinina et al., 2025).

Febrile Neutropenia and Sepsis Management: Empiric broad-spectrum anti-pseudomonal therapy (piperacillin-tazobactam or carbapenem) must start within 60 minutes of fever onset (Surviving Sepsis and IDSA guidelines). Vancomycin or linezolid is added for suspected Gram-positive infection, hemodynamic instability, or known colonization. In septic shock, aggressive fluid resuscitation, vasopressors, source control (e.g., central line removal), and G-CSF (filgrastim 5–10 μg/kg/day) to shorten neutropenia duration are standard. Antibiotic de-escalation or discontinuation upon neutrophil recovery and clinical stability is increasingly supported to reduce resistance and hospital stay (Herrera Rueda et al., 2024).

Respiratory Support: High-flow nasal cannula or non-invasive ventilation is preferred initially for hypoxia. Early intubation is indicated if no improvement within hours. For ARDS or DAH, lung-protective ventilation (tidal volume 6 mL/kg predicted body weight), prone positioning, and cautious corticosteroid use (e.g., methylprednisolone <250–500 mg/day equivalent for DAH) are employed. Bronchoalveolar lavage aids diagnosis.

Organ Support and Supportive Care: AKI management includes nephrotoxin avoidance, fluid optimization, and renal replacement therapy when indicated. Nutritional support (enteral preferred when possible; TPN otherwise) and multimodal analgesia for mucositis are critical. Hematologic support involves platelet transfusions (threshold $<10 \times 10^9$/L prophylactic or higher with bleeding) and red blood cell transfusions as needed. Engraftment syndrome is typically managed with corticosteroids (e.g., methylprednisolone 1–2 mg/kg/day) with rapid tapering.

Multidisciplinary Approach: Close collaboration among hematologists/transplant physicians, intensivists, infectious disease specialists, and organ-specific experts (neurology, rheumatology, pulmonology) improves outcomes. Early ICU consultation or transfer before overt multi-organ failure is associated with survival >70% (Stephens, 2019).

Recent data show that with modern protocols, 30-day morbidity-free survival after AHSCT for ADs exceeds 87–98% in experienced centers, with significant reductions in prolonged antibiotic use and hospital length of stay through structured de-escalation strategies.

Discussion. The agranulocytosis period following autologous hematopoietic stem cell transplantation (AHSCT) in patients with autoimmune diseases represents a uniquely vulnerable phase characterized by profound immunosuppression and systemic physiological stress. The findings of this review confirm that, despite significant advances in transplantation protocols, this early post-conditioning window remains the principal determinant of short-term morbidity and intensive care utilization.

A key observation is the persistently high incidence of infectious complications, particularly febrile neutropenia and bacterial sepsis, which continue to dominate the clinical landscape. This is consistent with the pathophysiological interplay between severe neutropenia, disruption of mucosal barriers, and microbial translocation. However, compared to earlier decades, the spectrum of infections appears to be shifting due to improved antimicrobial prophylaxis and infection control practices, with a relative increase in resistant organisms and opportunistic pathogens in selected high-risk subgroups. This underscores the importance of individualized antimicrobial strategies and antimicrobial stewardship during the neutropenic phase.

In parallel, non-infectious complications such as engraftment syndrome (ES) present an important diagnostic and therapeutic challenge. The overlap between ES and infectious syndromes often leads to diagnostic uncertainty, potentially delaying appropriate immunomodulatory treatment. In systemic sclerosis cohorts, where ES incidence is particularly high, early recognition based on clinical patterns and biomarker trends is crucial. The role of inflammatory biomarkers, including procalcitonin and emerging markers such as presepsin, may help differentiate infectious from non-infectious etiologies, although their utility requires further validation in prospective studies. Another important aspect highlighted in this review is the growing role of intensive care medicine in improving AHSCT outcomes. Early ICU involvement, rather than delayed transfer in the setting of multi-organ failure, has been associated with better survival outcomes. Advances in supportive care—including lung-

protective ventilation strategies, early use of high-flow oxygen therapy, optimized hemodynamic monitoring, and timely renal replacement therapy—have significantly contributed to reducing treatment-related mortality. Importantly, the integration of transplant teams with intensivists and infectious disease specialists has become a cornerstone of modern AHSCT programs.

The declining treatment-related mortality rates (<2% in experienced centers) reflect not only improvements in supportive care but also better patient selection and refinement of conditioning regimens. Avoidance of excessively toxic protocols, particularly in patients with pre-existing organ dysfunction, has played a crucial role in minimizing complications. Nevertheless, variability between centers remains, suggesting that institutional experience and adherence to standardized guidelines significantly influence outcomes. Despite these advances, several gaps remain. There is a need for standardized risk stratification models that incorporate disease-specific factors, conditioning intensity, and baseline organ function to better predict complications during the agranulocytosis phase. Additionally, prospective multicenter studies are required to evaluate optimal antimicrobial de-escalation strategies, biomarker-guided diagnostics, and ICU admission criteria. Addressing these gaps will be essential for further improving safety and expanding access to AHSCT in autoimmune diseases.

Conclusion. The agranulocytosis phase after AHSCT in autoimmune diseases remains a critical period associated with a high risk of both infectious and non-infectious complications. However, advances in prophylactic strategies, early diagnostic approaches, and intensive care management have substantially improved patient outcomes, reducing treatment-related mortality to historically low levels. Effective management during this phase relies on early recognition of complications, prompt initiation of evidence-based therapies, and a multidisciplinary approach integrating transplant specialists, intensivists, and infectious disease experts. Individualized care strategies—guided by patient risk profiles, disease characteristics, and evolving clinical data—are essential to optimize outcomes. Future progress in this field will depend on the development of predictive models, refinement of supportive care protocols, and incorporation of novel biomarkers to enhance diagnostic precision. With continued improvements in intensive care and transplant medicine, AHSCT is likely to become an

increasingly safe and widely applicable therapeutic option for patients with severe autoimmune diseases.

References:

1. Alexander, T. (2025). Autologous haematopoietic stem cell transplantation for autoimmune diseases. *Bone Marrow Transplantation*. https://doi.org/10.1038/s41409-025-02695-y
2. Daikeler, T., Tichelli, A., & Passweg, J. (2012). Complications of autologous hematopoietic stem cell transplantation for patients with autoimmune diseases. *Pediatric Research, 71*(2), 439–444. https://doi.org/10.1038/pr.2011.157
3. Dubinina, Y. N., et al. (2025). Practice of inflammatory biomarkers for prediction of infectious complications after autologous hematopoietic stem cell transplantation. *Oncohematology*.
4. Greco, R., et al. (2021). Hematopoietic stem cell transplantation for autoimmune diseases in the time of COVID-19. *EBMT guidelines*.
5. Herrera Rueda, G. A., et al. (2024). Evaluation of adherence, safety and effectiveness of an antibiotic de-escalation strategy in patients with febrile neutropenia during autologous hematopoietic stem cell transplantation. *Journal of Bone Marrow Transplantation and Cellular Therapy, 5*(2).
6. Kalincik, T., et al. (2023). AHSCT vs fingolimod, natalizumab, and ocrelizumab in highly active multiple sclerosis. *JAMA Neurology*. https://doi.org/10.1001/jamaneurol.2023.1542
7. Levin, D., et al. (2022). Hematopoietic cell transplantation for systemic sclerosis. *Cells, 11*(23), 3912. https://doi.org/10.3390/cells11233912
8. Muraro, P. A., et al. (2017). Long-term outcomes after autologous hematopoietic stem cell transplantation for multiple sclerosis. *JAMA Neurology, 74*(4), 459–469. https://doi.org/10.1001/jamaneurol.2016.5867
9. Park, S. H., et al. (2006). Current trends of infectious complications following hematopoietic stem cell transplantation. *The Korean Journal of Hematology*.
10. Sieiro Santos, C., et al. (2025). Autologous hematopoietic stem cell transplantation in autoimmune diseases. *ACR Open Rheumatology*. https://doi.org/10.1002/acr2.70131

11. Stephens, R. S. (2019). ICU complications of hematopoietic stem cell transplant. In *Evidence-based critical care*. Springer.

12. Strunz, P. P., et al. (2021). Immunological adverse events after autologous hematopoietic stem cell transplantation in systemic sclerosis. *Frontiers in Immunology*.

13. Gazkhanovna, M. A., Makhmatovich, A. K., & Utkirovich, D. U. (2022). Clinical efficacy of extracorporeal and intravascular hemocorrection methods in psoriasis. Academicia: An International Multidisciplinary Research Journal, 12(2), 313-318.

14. Madasheva, A. G., & Abdiev, K. M. (2023). Blood transfusion therapy in patients with vitamin B12 deficiency anemia after resection of 2/3 of the stomach. Science and Education, 4(5), 407-412.

15. Мадашева, А. Г., & Жураева, М. З. (2019). Биохимические показатели и комплексное лечение больных псориазом с лечебным плазмаферезом. Достижения науки и образования, (10 (51)), 78-82.

16. Мадашева, А., Бергер, И., Махмудова, А., Абдиев, К., & Амерова, Д. (2025). Лабораторная диагностика. восточная европа. лабораторная диагностика, 14(1), 87-96.

17. Мадашева, А. Г. (2022). Клинико-неврологические изменения у больных гемофилией с мышечными патологиями. Science and Education, 3(12), 175-181.

18. Мадашева, А. Г. (2022). Коррекция диффузной алопеции при железодефицитной анемии. Science and Education, 3(12), 231-236.

19. Мадашева, А. Г., Дадажанов, У. Д., Абдиев, К. М., Маматкулова, Ф. Х., & Махмудова, А. Д. (2019). Динамика электронейромиографических показателей и эффективность электрической стимуляции мышц у больных гемофилией с мышечными атрофиями. Достижения науки и образования, (10 (51)), 26-30.