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EMERGING TRENDS IN STEM CELL THERAPY FOR BLOOD DISORDERS: FROM BLOOD BANKING TO HEMATOLOGICAL MALIGNANCIES

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ABSTRACT
Stem cell therapy (SCT) has become a cornerstone of regenerative hematology, offering promising therapeutic and methods that may be able to treat a variety of blood problems, both malignant and non-malignant. Advances in blood banking, hematopoietic stem cell transplantation (HSCT), and regenerative medicine have substantially expanded the clinical utility of stem cell-based therapies. The goal of this review is to offer a thorough summary of emerging trends in SCT for blood disorders, with emphasis on blood banking, transplantation strategies, therapeutic applications, and recent technological innovations shaping modern hematological practice. hematopoietic stem cells (HSCs) derived from bone marrow, peripheral blood, umbilical cord blood, and induced pluripotent stem cells have significantly improved the treatment of haematological cancers, bone marrow failure syndromes, and hereditary blood disorders. Progress in stem cell collection, cryopreservation, donor selection, and transplantation has enhanced engraftment, safety, and clinical outcomes. Emerging technologies, including gene editing, ex vivo stem cell expansion, stem cell engineering, artificial intelligence, and precision medicine, are driving the development of personalized regenerative therapies. Nevertheless, challenges related to Graft-versus-host disease, treatment costs, donor availability, long-term safety, ethical governance, and healthcare inequities continue to influence clinical implementation. SCT is redefining the management of blood disorders through continuous advances in transplantation biology, regenerative medicine, and precision therapeutics. Ongoing multidisciplinary research, technological innovation, and equitable healthcare strategies are expected to further improve treatment efficacy, accessibility, and long-term patient results.

KEYWORDS: hematopoietic stem cells, Blood banking, Hematopoietic stem cell transplantation, Hematological malignancies, Regenerative medicine, Gene editing.

1. INTRODUCTION
Blood disorders are a significant worldwide health issue, and a broad range of benign and malignant diseases that destroy hematopoiesis, immune response, and general physiological homeostasis is covered. These disorders are genetic ones (sickle cell disease, thalassemia), acquired ones (aplastic anemia, etc.), and hematological malignancies (leukemia, lymphoma, multiple myeloma, etc.). Despite the improvements in chemotherapy, targeted therapy, immunotherapy, and supportive care, which have increased patient survival, most disorders still need definitive regenerative therapy to restore normal hematopoietic functions. It is thus seen that stem cell therapy (SCT) has become one of the most promising therapeutic modalities in the modern hematology that promises long-term remission of the disease and in some special cases, a full cure (Aly, 2020).
Over the last few decades, SCT has transformed the experimental bone marrow transplant into a highly complex clinical field with a variety of sources of stem cells, improved transplantation regimens, and regeneration technologies. Hematopoeietic stem cells (HSCs) have the special ability of self-rejuvenation and multilineage distinction, which allows them to produce immune and blood cells throughout their lifetime. Such biological properties made HSCs the foundation of therapy in various hematological diseases and have spurred ongoing advances in transplantation and regenerative medicine (Okeke et al., 2021). Recently, the development of stem cell engineering, gene-editing technologies, induced pluripotent stem cells, and precision medicine has only extended the therapeutic potential of stem cell-based interventions, providing fresh prospects of personalized treatment of a large number of diseases (Abusalah et al., 2024).
The other key ingredient of successful SCT is the creation of an effective blood banking and stem cell preservation systems. The development of cord blood banks has greatly enhanced the availability of access to the HSCs, which could

be utilized in transplantation, especially in individuals without completely matched donations. The umbilical cord blood is currently an appealing source of stem cells due to its rapid availability, reduced occurrence of severe graft-versus-human disease, and higher human leukocyte antigen mismatch tolerance than traditional sources of donor blood (Kurtzberg, 2017). Advances in the collection, processing, long-term storage, and quality control of stem cells have also increased the clinical utility of banked stem cells and underlies the growing use of regenerative medicine and cellular therapies (Mayani et al., 2020).

Clinical importance of HSCT has been on the rise due to the enhancement of the donor registries, techniques of transplantation, supportive care, and international collaboration networks. The transplantation operation worldwide has gradually grown in the last 30 years, which is indicative of the general clinical evidence and enhanced treatment results of both malignant and non-malignant blood diseases (Passweg et al., 2021). Simultaneously, the application of SCT to the treatment of blood cancers has revolutionized the treatment interventions by offering curative means to diseases that were previously linked with a high likelihood of poor prognosis and poor survival after treatment (Rahimi Darehbagh & Rezaei, 2024).

The review is a thorough discussion of the emerging trends in SCT of blood disorders, which starts with the biological background of HSCs and the usage of blood banking in the preservation of stem cells. It then addresses the existing transplantation practices, their current use in nonmalignant and malignant hematological disorders, the recent technological developments, and future prospects which are likely to further develop regenerative hematology and give better patient outcomes.

2. Stem Cells in Hematology: Biological Basis and Therapeutic Potential

Stem cells are the basis of regenerative haematology as their exceptional ability to regenerate the hematopoietic system and provide normal blood cell formation. The extraordinary potential of stem cells in terms of self-renewal, multilineage differentiation, and long-term hematopoietic reconstitution revolutionized the approach to the treatment of genetic and acquired diseases affecting the blood. In the last few decades, significant progress in stem cell biology has increased the pool of stem cells usable in clinic, as well as our knowledge of the molecular basis of hematopoiesis. This progress contributed to an increased efficiency of HSCT, and novel regenerative approaches to blood disorders.

2.1 Types of Stem Cells Used in Blood Disorders

Numerous blood disorders are being treated with different types of stem cells, each having its own biological properties, harvesting methods, immune profile, and clinical uses. Selection of the right kind of stem cell depends upon the nature of the disease, the suitability of the donor, the technique of transplantation, and the expected results. These stem cell populations have opened up new vistas for regenerative hematology.

2.1.1 HSCs (HSCs)

The multipotent stem cells known as HSCs are capable to regenerate themselves throughout life as well as differentiate into all mature blood cell types, namely erythrocytes, leukocytes, and platelets. HSCs constitute the primary constituent of HSCT, representing the standard treatment approach for many hereditary and acquired blood diseases. Having the capacity to restore normal hematopoiesis after bone marrow failure, high dose chemotherapy, or genetic defects, HSCs have become essential for hematological diseases treatment. The regenerative properties of HSCs are still inspiring the research in the sphere to create new therapy approaches for transplantations (Rao et al., 2022).

2.1.2 Umbilical Cord Blood Stem Cells

Cord blood provides a critical alternative to traditional sources of HSCs due to its superior proliferative likely, ease of harvesting, immediate availability, and reduced immunogenic properties. Cord blood transplantation offers the advantage of reduced risks of developing serious cases of graft-versus-host disease and higher toleration of mismatches in human leukocyte antigen in contrast to bone marrow transplantation from donors. Recent developments in cord blood banking, in vitro expansion, and cellular reprogramming have greatly improved the applicability of cord blood-derived stem cells for the treatment of pediatric and adult hematologic conditions (Berglund et al., 2017).

2.1.3 Bone Marrow-Derived Stem Cells

The bone marrow is among the most researched and frequently employed sources of HSCs for allogenic transplantation. Bone marrow hosts a highly enriched number of primitive HSCs surrounded by specific stromal and mesenchymal cells that control stem cell survival, renewal, and differentiation. The bone marrow microenvironment has a crucial effect on maintaining the functionality of stem cells and their ability to perform hematopoiesis. Despite the need for an invasive method to collect bone marrow samples, it guarantees successful engraftment and hematopoietic recovery, which makes bone marrow a preferable source of HSCs for various diseases (Colom Díaz et al., 2023).

2.1.4 Peripheral Blood Stem Cells

The mobilisation of HSCs from the bone marrow to peripheral blood via pharmacological techniques is a component of the peripheral blood stem cell group. The procedure has gained popularity because it allows for easy collection of stem cells without any major invasion, and it provides a better yield compared to traditional methods of harvesting of stem cells from the bone marrow. Peripheral blood stem cell transplantation is characterized by quick platelet and neutrophil recovery, faster immune recovery and shorter hospital stays, and that is why it has gained popularity in hematopoietic

transplantation programs among adults. Mobilization and function of HSCs in the circulation are regulated by inflammatory signaling and cytokines (Pietras, 2017).

2.1.5 Induced Pluripotent Stem Cells (iPSCs)

One of the most exciting advances in regenerative medicine is the use of induced pluripotent stem cells, or iPSCs. They are derived from mature somatic cells reprogramming to be induced into a pluripotent state, thus becoming capable of developing into hematopoietic progenitors and various other cell types. The fact that iPSCs are patient-specific provides many possibilities regarding disease modeling, gene editing, personalized medicine, and eventual autologous transplantations while avoiding the ethical problems of using embryonic stem cells. While there is still much to explore clinically about iPSCs, they keep growing in terms of their medical application potential (Ilic & Ogilvie, 2022).

2.2 Biological Characteristics and Mechanisms of HSCs

The biological characteristics of stromal cells and the sophisticated molecular mechanisms that control their activity determine the therapeutic efficacy of HSCT not only because of the source of the stem cells but also because of the intrinsic biological traits of this type of cell. The HSCs ensure a system of lifelong blood cell production by a strictly regulated self-renewal, differentiation, homing and engraftment of donors after transplantation through interaction with the bone marrow microenvironment. A combination of these mutually related biological processes defines hematopoietic homeostasis, regenerative ability and long-term transplantation success.

An important feature of HSCs is the possibility of self-renewal and at the same time to create lineage-committed progenitor cells which develop into all the mature types of blood cells. The balance sustains the maintenance of the pool of stem cells throughout life but also replenishes erythroid, myeloid and lymphoid progenitors as needed by the body. The HSCs activity is controlled in the specialized Stromal cells, endothelial cells, osteoblasts, mesenchymal stem cells, extracellular matrix elements, and different cytokines make up the bone marrow microenvironment, also known as the haematopoietic niche that combine to sustain stem cell quiescence, proliferation, survival, and lineage commitment. After transplantation, effective homing and engraftment entails transplanted stem cells migrating via chemokine-induced signal transduction, binding to bone marrow niches and developing sustainable hematopoiesis. Genetic defects or disturbed cellular signaling disrupt these regulatory processes and may disrupt stem cell activity, break engraftment, and play a role in the onset and progression of hematological malignancies (Saez et al., 2017). These key biological processes that regulate the functionality of hematopoietic stem cell are outlined in Figure 1.

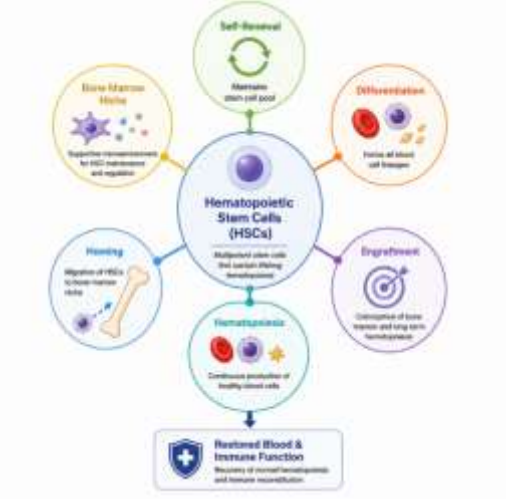

Figure 1. Biological Functions of HSCs

HSCs sustain the proper functioning of blood production by means of an array of integrated activities including self-renewal, differentiation, interactions with bone marrow microenvironment, homing and engraftment, as demonstrated in Figure 1. It is owing to these mechanisms that the HSCs are able to continuously produce healthy blood cells as well as regenerate immune system after transplantation. It is the foundation of the process of HSCT.

3. Blood Banking and Stem Cell Preservation

Blood banking and stem cell storage act as the bedrock for successful HSCT by providing high-quality stromal cell products for clinical use. Innovations in techniques such as harvesting, storage, and cryopreservation as well as donor screening have greatly contributed to improved success rates and increased global accessibility to stromal cell treatments. The expansion of standardized banking techniques, strict quality control standards, and donor registry systems has improved the safety, efficacy, and preservation of HSCs. Blood banking has increasingly become an vital part of reformative medicine and the emerging field of cellular therapy, playing a crucial role in personalized treatment options for various hematological diseases.

3.1 Evolution of Blood and Cord Blood Banking

The advent of blood and cord blood banking has revolutionized HSCTs through offering easily accessible sources of stem cells for patients needing regenerative treatment. Initially concentrating on the traditional process of blood banking, banking techniques have since been enhanced to include cord blood banking after the realization that umbilical cord blood

is rich in HSCs. Standardized procedures for blood banking, donor screening, and quality assurance have greatly improved the safety and use of blood samples for regenerative purposes. Cord blood banking has become an important aspect of modern transplantation practice through improving donor accessibility and regenerative medicine and cell therapy (Armitage, 2016). The continued improvement of blood banking practices has further made the use of cord blood more important in therapy. There has also been a significant improvement in public knowledge concerning cord blood donation which has increased their involvement in blood banking practices (Pandey et al., 2016).

3.2 Stem Cell Collection and Processing

The successful use of stromal cell transplantation is largely influenced by the efficiency of stem cells harvesting and processing while ensuring their survival and functional competency. Bone marrow, peripheral blood, or umbilical cord blood can all be used to extract cells depending on well-established methods intended to achieve higher cell yields with minimal contamination. After stem cell harvests, these cells are processed in terms of volume reduction, cell separation, viability, screening for infectious diseases, and quality control prior to long-term storage or transplantation. Such laboratory standards provide the best quality of the graft and facilitate transplantation efficacy. Further improvements due to technological advances contributed to optimization of processing and reduction of cellular injury during the process making stem cell products more efficacious in the treatment of hematological diseases (Shearer et al., 2017). Fresh umbilical cord blood is a unique source of cells since it contains numerous multipotent stem cells and provides an easy way for their harvesting right after birth (Devi et al., 2023).

3.3 Cryopreservation and Storage Technologies

Cryopreservation is an essential part of the stem cell banking, which allows maintaining the cellular viability, functionality, and regenerative potential of the cells during long periods. Controlled-rate freezing and special cryoprotective agents are modern cryopreservation methods that are used to reduce the amount of ice in the cell and cell injury caused by the low-temperature storage. These technological developments have significantly enhanced the recovery and successful transplantation of post-thaw cells and this means that stem cells can be stored and still be biologically viable over a long time. The constant improvements in the storage technologies also help to provide the quality assurance, minimize the damage associated with the processing, and further increase the efficiency of the stem cell banking systems (Dessels et al., 2018). Moreover, the new uses of induced pluripotent stem cell technology have widened the horizons of blood banking, as they provide new opportunities in preserving cells on a patient-specific basis and in future regenerative medicine (Focosi & Pistello, 2016).

3.4 Public versus Private Cord Blood Banking

This blood banking can be broadly classified into different types of banking system: public and private banking which have different clinical and societal applications. Public cord blood banks store the donated units on behalf of unrelated recipients, thereby increasing the supply of stem cell grafts to patients who need transplantation, and facilitating international donor registries. Conversely, the private banks do not discard the cord blood unless it can be used in the future by the donor or relatives, but the chances of autologous use are rather low. Generally, public banking has been said to be more advantageous on a public health level since it ensures maximum accessibility of resources and equitable utilization of donors. However, both banking models play a part in the increased infrastructure in regenerative medicine and transplantation. They both have their own pros and cons, and it is crucial to assess them carefully to make informed decisions by medical workers and future parents (Narayanan and Phadke, 2019). The two systems will continue to be combined further in the future to the changing global stem cell banking networks (Querol et al., 2021).

3.5 Donor Selection, HLA Matching, and Ethical Considerations

The correct choice of donors is the key to the successful HSCT, where human leukocyte antigen (HLA) compatibility can be central to the reduction of graft refusal and graft-versus-human disease and the enhancement of long-term survival. Thorough evaluation of donors will involve review of medical history, screening of infectious diseases, genetic compatibility, and overall donor fitness to make sure that the patient will be safe and achieve the best results of transplantation. Recommendations provided by international consortiums have also provided a standardization of eligibility criteria in donors, to enhance uniformity in transplantation facilities around the globe (Worel et al., 2022). In addition to the scientific factors, ethical concerns are still paramount to stem cell banking and transplantation such as informed consent, privacy of the donor, fair access to donor registries and prudent use of scarce stem cell resources. These ethical issues can be addressed by providing clear regulatory frameworks and multilateral partnerships that will guarantee fairness, community trust and long-term growth of the global stem cell donor registries (Aljurf et al., 2019). The major stem cell sources, banking approaches, and preservation characteristics are shown in Table 1.

Table 1. Comparison of Stem Cell Banking and Preservation Strategies

Feature	Bone Marrow	Peripheral Blood	Cord Blood	Key References
Stem cell source	Bone marrow	Mobilized blood	Umbilical cord	Shearer et al., 2017; Devi et al., 2023
Collection	Invasive	Leukapheresis	Post-delivery	Shearer et al., 2017
Cell dose	Moderate	High	Low	Devi et al., 2023
Engraftment	Moderate	Fast	Slow	Dessels et al., 2018

HLA matching	Strict	Strict	More flexible	Worel et al., 2022
Major advantage	Durable graft	Rapid recovery	Lower GVHD	Querol et al., 2021
Major limitation	Surgical harvest	Chronic GVHD risk	Low cell dose	Narayanan & Phadke, 2019

4. HSCT: Current Clinical Practice

HSCT is still the mainstay of treatment for many blood disorders, both malignant and non-cancerous. During the last few decades, considerable developments have been made in transplantation methods, donors, preparation regimens, and supportive treatment, which have led to the increase in patients' survival and broadening the scope of indications for HSCT. The current approach to transplantation includes different types of donors and treatment approaches tailored for each particular patient. Further developments in transplantation science have helped to cement the role of HSCT as a key aspect of regenerative hematology.

4.1 Types of HSCT

Various types of HSCT have been established to treat the various therapeutic needs of patients with blood disorders. The type of transplantation that is selected depends on the nature of the disease, availability of donors, genetic conformity, and the expected treatment results.

Autologous transplantation entails harvesting and returning HSCs of a patient after a high dose chemotherapy. This is an effective method of reducing the risk of graft-versed-hormone disease and offers effective recovery of hematopoiesis and is commonly used in the management of multiple myeloma and some lymphomas. In contrast, allogeneic transplantation involves the use of stem cells derived out of a genetically comparable donor, and it has the added advantage of the graft-versus-leukemia effect and is indeed the treatment of choice in the majority of leukemias and inherited hematologic diseases (Juric et al., 2016).

Haploidentical transplantation with the use of partially matched family donors has become a viable option where fully matched donors are not available for the patients. The advancement of immunosuppressive protocols and graft manipulation have significantly increased the success of transplantation, and the practice has become common in various parts of the world (Apperley et al., 2016). Another useful alternative source of donors is the cord blood transplantation due to its quick availability and less prone to severe graft-versus-host disease despite slower hematopoietic recovery (Ballen, 2017). The trend of the use of haploidentical transplantation keeps growing as evidenced by growing international experience of the growing role of the practice in modern-day clinical practice (Passweg et al., 2017).

4.2 Conditioning Regimens and Engraftment

The process of conditioning is a vital prerequisite for stem cell transplantation, which consists of elimination of malignancies, immunosuppression of the recipient, and making bone marrow space for donor cells to engraft into. The choice of either myeloablative or reduced-intensity conditioning, as well as the application of irradiation, depends on the condition of the patient, age, and overall health. Modern developments in stem cell transplantation have been centered on increasing efficiency and lowering adverse effects of treatment. New approaches, like expansion of stem cells from cord blood ex vivo, have shown promising findings in promoting hematopoietic recovery and decreasing side effects after transplantation (Cohen et al., 2020). However, engraftment is also determined by the quality of donor cells and recipient marrow microenvironment because of the potential involvement of clonal hematopoiesis from the donor cells into the hematological outcome after transplantation (Gibson et al., 2017).

4.3 Donor Selection Strategies

Choosing the right donors is one of the most crucial elements of success in the HSCT process. HLA compatibility still serves as the basis for donor selection since good compatibility will lead to lower chances of mortality, graft against host disease, graft failure, and increased survival rates. Modern donor selection includes additional aspects such as patient's age, characteristics of his/her disease, health condition of the donor, cytomegalovirus serostatus, source of stem cells and general transplantation risk assessment. The international guidelines on donor selection and transplantation indications are continuously developed in order to allow more personalized approaches in clinical practice (Zhang et al., 2021). At the same time, the world donor registries and transplantation networks have increased donor availability significantly (Niederwieser et al., 2016).

4.4 Clinical Outcomes and Current Challenges

Outcomes of HSCT have been greatly enhanced owing to innovations in identification of donors, conditioning programs, avoidance of infections, supportive care, and monitoring following transplantation. The total number of HSCTs has kept increasing every year due to new clinical indications and increased availability via alternative donors' approaches and international transplant programs (Niederwieser et al., 2021). While substantial progress has been made in transplantation medicine, there are still some issues that should be addressed, like, graft-versus-host disease, infections, disease recurrence, immune recovery problems, and treatment-related morbidity. Even though mortality rates of patients who undergo HSCT have significantly decreased during recent years as a result of advances in clinical practice, more work needs to be done for even greater safety of transplants, better patient survival and higher quality of life after HSCT (Penack et al., 2020). The entire workflow of HSCT is shown in Figure 2.

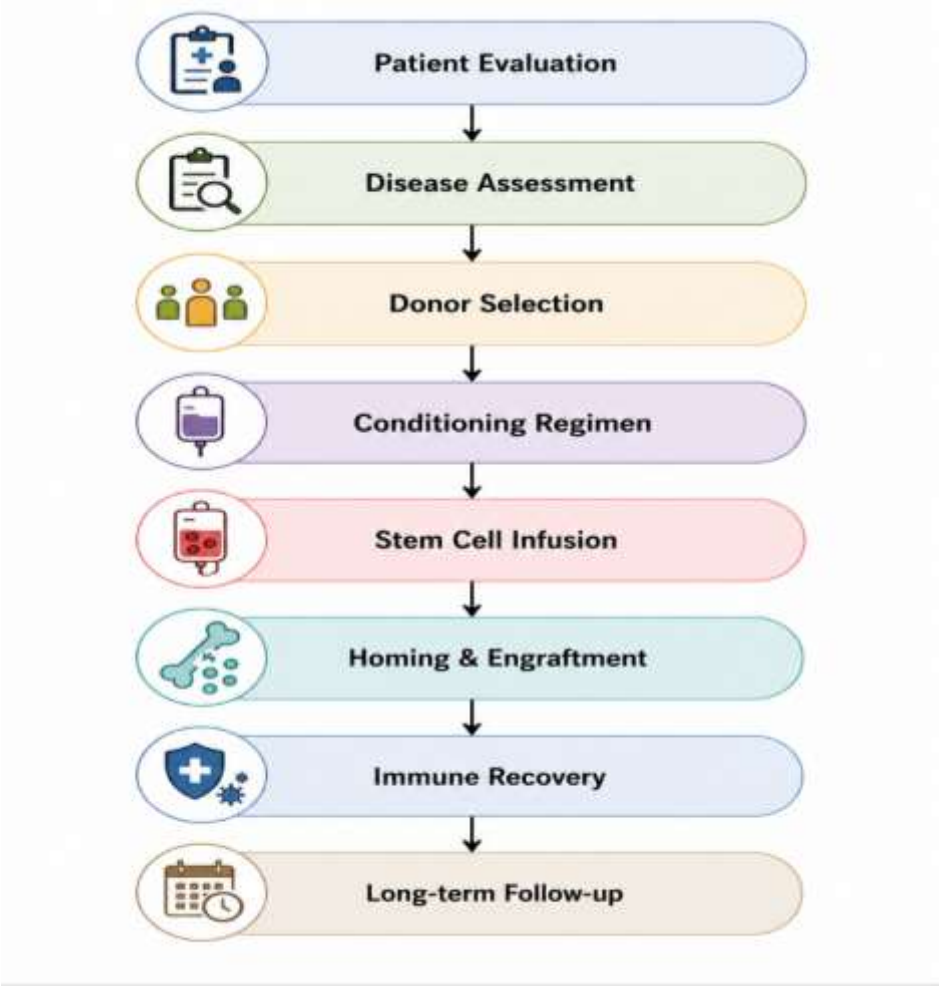

Figure 2. HSCT Pathway

HSCT has a well-organised clinical pathway, as shown in Figure 2, which starts with thorough patient assessment and evaluation of the disease, selection of the donor and relevant conditioning therapy. Following stem cell infusion, hematopoiesis and immune function is restored by successful homing and engraftment. Post-transplant follow-up and continuous monitoring is a lasting practice required to assess engraftment, identify complications like graft-versus-host disease or relapse and maximize long-term clinical outcomes in individuals undergoing HSCT.

5. SCT for Non-Malignant Blood Disorders

SCT is now being considered a significant curative treatment to various non-malignant blood diseases which are caused by inherited mutations, bone marrow failure, immune dysfunction or metabolic abnormalities. In contrast to supportive treatments, which primarily manage symptoms and complications of diseases, HSCT may substitute the damaged hematopoietic cells with normal donor hematopoietic cells and re-establish normal blood and immune functioning. The advances in the selection of donors, conditioning programs, graft manipulation, prevention of infection and after-transplant care have broadened the application of transplantation to a broader group of patients. New possibilities are also emerging with the use of emerging gene-corrected autologous stem cell approaches that can offer new possibilities to individuals who do not have appropriate donors or who have a significant risk of adverse effects of traditional allogeneic transplantation.

5.1 Sickle Cell Disease

Chronic haemolysis, recurrent vaso-occlusive crises, gradual organ damage, and a reduced survival rate are the hallmarks of sickle cell disease, an autosomal recessive hereditary blood illness. Allogeneic haematopoietic stem cell transplantation, which replaces the patient's aberrant blood-forming cells with donor cells capable of creating normal haemoglobin, is an established treatment for sickle cell disease. Improvements in less toxic regimens, haploidentical transplants, and gene editing techniques have allowed for more treatment opportunities than just patients who have fully matched siblings (de la Fuente et al., 2020). The emerging novel graft product omidubicel stem cells could enhance cell dose and speed up hematopoietic reconstitution but still need further investigation on their efficacy and safety (Parikh et al., 2021).

5.2 Thalassemia

Thalassemia is a genetic condition where there is abnormal hemoglobin production leading to anemia and other complications like iron overload and end-organ dysfunction. HSCT provides the opportunity for curing thalassemia involves substituting good haematopoiesis from a donor for the patient's malfunctioning erythroid cells. Success rates are

usually better when the patient is young, has minimal iron-induced damage to their organs, and a well-matched donor. Better conditioning regimens, HLA matching, support care, and alternative donor transplant have helped to increase the number of patients undergoing HSCT. Local stem cell transplant centers have been another factor responsible for increased HSCT in inherited blood disorders even though treatment-related toxicity, donor issues, and disparity in access to healthcare continue to be problems (Chang et al., 2022).

5.3 Aplastic Anemia and Bone Marrow Failure Syndromes

Aplastic anemia and syndromes of bone marrow failure are identified by a lack of production of one or more blood cell lineages, leading to anemia, infection and bleeding complications. Allogeneic HSCT is able to recover the marrow function by repairing the damaged or defective hematopoietic system with healthy donor stem cells. Matched sibling donor transplantation is usually used with young patients who are eligible but when matched sibling donors are unavailable, unrelated, haploidentical, and cord blood grafts should be used. Better infrastructure in transplantation and clinical skills within the Asia-Pacific region have facilitated broader applications of alternative donors to acquired and inherited marrow failure diseases (Iida et al., 2019). Still, the failure of grafts, infection and immune complications are factors that still affect the outcome.

5.4 Primary Immunodeficiency Disorders

The category of primary immunodeficiency illnesses is diverse of inherited disorders where defects in the development or function of immune-cells cause severe, recurrent, or opportunistic infections. The transplantation of HSCs can offer a solution to a permanent cure because it is possible to replace the malfunctioning immune and hematopoietic cells with normal donor-grown ones. Diagnosis of the case at the initial stage, control of active infection, the selection of the donor, and individual conditioning are the key to successful results. The transplantation activity of children has grown significantly with specialized centers becoming more competent in handling the complicated hematological and immune diseases in childhood (Khandelwal et al., 2017). Nevertheless, the delay in diagnosis, the lack of donors, graft-versus-human disease, and the toxicity of the treatment are also significant issues, especially at the facilities with limited access to specialized transplantation services.

5.5 Inherited Metabolic and Genetic Hematological Disorders

The use of hematopoietic SCT is increasingly being used in the therapy of the few inherited metabolic and genetic disorders where donor-derived cells can repair missing enzymes, correct defective hematopoiesis or limit progressive tissue damage. Possible signs comprise inherited marrow failure syndromes, hemoglobinopathies, lysosomal storage disorders and other monogenic diseases that impact blood or immune-cell functioning. Early transplantation can help to avoid irreversible neurologic, hepatic or skeletal issues in suitable patients. Other areas of regenerative medicine under investigation include gene-corrected autologous stem cells, pluripotent stem cell-based products, and tissue-engineered therapies to address donor constraints and minimize immune issues. It will be important to continue to invest in research, manufacturing capacity, regulatory oversight, and clinical infrastructure to translate these therapies to larger practice (Imran et al., 2022). Table 2 below shows the main types of benign blood diseases treated using hematopoietic stem cell transplant and the key health benefits that are provided by the treatments. It also demonstrates how increasingly the use of hematopoietic stem cell transplant is being regarded as a potential cure for many diseases.

Table 2. Clinical Applications of HSCT in Major Non-Malignant Blood Disorders

Disease	Preferred Stem Cell Strategy	Major Clinical Benefit	Key References
Sickle cell disease	Allogeneic HSCT	Curative therapy	de la Fuente et al., 2020; Parikh et al., 2021
Thalassemia	Allogeneic HSCT	Transfusion independence	Chang et al., 2022
Aplastic anemia	Matched donor HSCT	Marrow restoration	Iida et al., 2019
Primary immunodeficiency	Early HSCT	Immune reconstitution	Khandelwal et al., 2017
Genetic/metabolic disorders	HSCT ± gene-corrected cells	Disease correction	Imran et al., 2022

6. SCT for Hematological Malignancies

Hematological malignancies represent a wide range of cancers derived from either hematopoietic or lymphoid tissues. Hematological cancers include leukemia, lymphoma, multiple myeloma, myelodysplasia, and myeloproliferative neoplasms. While the use of targeted agents, immunotherapy, and molecular therapy has significantly increased the efficacy of treatment, HSCT is currently the sole curable treatment option for many types of hematological malignancies that are high risk or have undergone relapse. Improvements in the selection of donors, conditioning protocols, supportive care, and follow-up care have ensured that stem cell transplantation continues to be used as an effective form of treatment in hematological oncology.

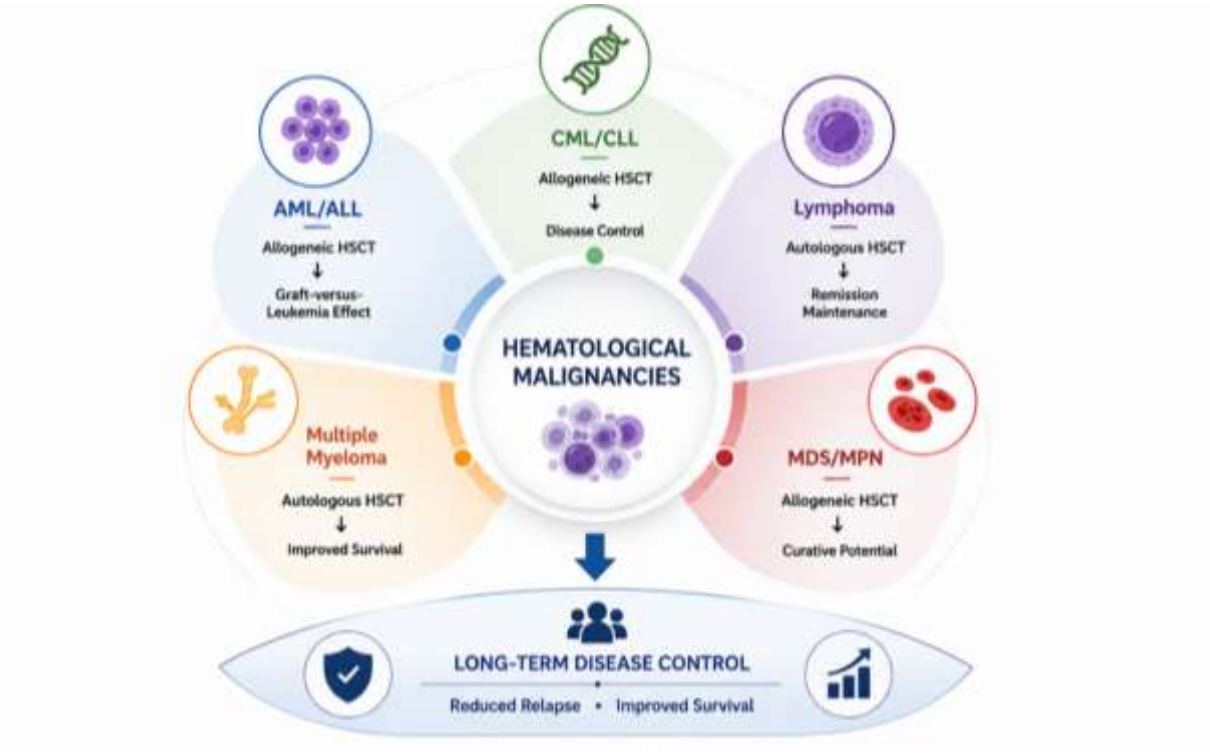

Figure 3. SCT Across Major Hematological Malignancies

As shown in Figure 3, transplant techniques for HSCs differ depending on the nature of the hematological malignancy. In the case of acute leukemias, chronic leukemias, and myelodysplasia/myeloproliferation syndromes, allogeneic HSCT is the method of choice; however, autologous HSCT is more often used in lymphomas and multiple myeloma. Such disease-oriented protocols facilitate better remissions, more sustained disease control, decreased relapses, and greater survival.

6.1 Acute Leukemia (AML and ALL)

Both acute lymphoblastic leukaemia (ALL) and acute myeloid leukaemia (AML) are aggressive hematological malignancies that are associated with unchecked proliferation of immature hematopoietic cells that inhibit normal bone marrow functions. Allogeneic HSCT is most likely to offer patients with unfavourable cytogenetic profiles and high-risk conditions, or relapsed leukemia the best chance of long-term remission due to complete hematopoietic replacement and the graft-versus-leukemia effect. Selection of bone marrow or peripheral blood stem cell grafts is determined by the nature of the disease, availability of donor and expected complications of transplantation. The existing research shows that both graft sources are effective in controlling the disease, but there are differences in the kinetics of engraftment, graft-versus-host disease, and long-term clinical outcomes, which highlight the need to consider individualized transplantation plans (Kiene et al., 2024).

6.2 Chronic Leukemia (CML and CLL)

With the emergence of tyrosine kinase inhibitors and targeted drugs, the treatment approach for CML and CLL has greatly evolved, and hematopoietic stem cell transplant is no longer indicated on a regular basis. However, allogeneic transplant still represents a viable treatment modality for patients with drug resistant disease, acceleration phase CML, and high risk CLL. Since a successful allogeneic transplant is associated with a number of complications, including infections, due to immunosuppression, which renders the patient susceptible to viral infections and liver damage, comprehensive guidelines for the diagnosis and treatment of viral hepatitis have been incorporated into the stem cell transplant protocol for patients with hematological malignancy (Mallet et al., 2016).

6.3 Lymphomas

Stem cell transplantation still remains significant in the treatment of the relapsed or refractive Hodgkin and non-Hodgkin lymphomas. Autologous transplantation is often employed after high dose chemotherapy to solidify remission and allogenic transplantation can be entertained in patients with recurrent disease or poor prognostic characteristics due to its graft-versus-lymphoma effect. Although there have been developments in supportive care, transplant recipients are still susceptible to opportunistic infections due to extended immunosuppression. Although mycobacterial infections are relatively rare, they may be a major cause of morbidity and mortality in such patients, which makes timely detection, prevention, and treatment of the infection based on the evidence particularly important during the transplantation period (Bergeron et al., 2022).

6.4 Multiple Myeloma

A plasma cell cancer called multiple myeloma occurs where autologous HSCs transplant is one of the regularly used treatments in the first line treatment of selected patients. Combined with contemporary induction and maintenance

therapies, high-dose chemotherapy and stem cell rescue considerably increases progression-free survival and treatment responses. Ongoing advances in transplantation methodology, supportive care, and selection of patients have led to the rise in the activity of transplantation globally and the fact that HSCT has become a part of overall management of myeloma. European surveys of transplantation have reported a stable increase in transplantation activity, indicating increased clinical acceptance and enhancing treatment outcomes in a variety of hematological malignancies, such as multiple myeloma (Passweg et al., 2016).

6.5 Myelodysplastic Syndromes and Myeloproliferative Neoplasms

The clonal hematopoietic diseases include myelodysplastic syndromes (MDS) and myeloproliferative neoplasma (MPNs) which pose different risks of progressive bone marrow failure and acute leukemia transformation. The only currently established curative therapy in selected high-risk patients is allogeneic HSCT, but it will only be successful when patient selection is taken into consideration and long-term post-transplant surveillance. Viral infections, especially cytomegalovirus reactivation, should be managed effectively to decrease morbidity and mortality in these immunocompromised patients following transplantation (Ljungman et al., 2019). Moreover, the growing awareness of therapy-associated clonal hematopoiesis has enhanced disease progression and poor clinical outcomes, and it enables a more accurate risk evaluation prior to transplantation (Coombs et al., 2017). The use of appropriate transfusion strategies is also a significant part of supportive care in the course of intensive treatment and transplantation, which helps to increase patient safety and clinical outcomes (Estcourt et al., 2017).

7. Emerging Trends in SCT

The future of hematological therapies is changing due to the rapid developments in the field of stem cell biology, regenerative medicine, and biomedical engineering. New technologies are now shifting away to standard HSCT and on to customized, gene-targeted and programmable cellular treatments that can enhance treatment response whilst reducing the side effects. Gene editing, induced pluripotent stem cells, ex vivo stem cell expansion, artificial intelligence, and advanced cell engineering are all innovations that are increasing the number of therapeutic options in treating both malignant and non-malignant blood diseases. All these advances will likely enhance the availability of donors, maximize the results of transplantations, and hasten the shift towards precision regenerative hematology.

bOne of the most promising developments in SCT has been the development of gene editing which allows the correction of the genetic mutations that cause diseases with high accuracy before the transplantation. CRISPR-Cas9 and other genome-editing systems allow the targeted editing of HSCs, potentially providing curative therapies to inherited blood diseases, and eliminating reliance on allogenic donors. Personalized regenerative therapy is becoming more and more possible as the risks of graft-versus-host disease and immune rejection are reduced by autologous transplantation of gene-corrected stem cells. Genetic modifications to pluripotent stem cells have shown promising safety and efficacy in recent clinical trials, making gene-corrected stem cell therapies with genetic modifications a viable option to translate into clinical practice (Kim et al., 2022).

7.2 Induced Pluripotent Stem Cells and Regenerative Hematology

The induced pluripotent stem cells (iPSCs) have broadened the horizons of regenerative hematology because the cells offer an unlimited source of patient-specific cells that can be differentiated into hematopoietic and other specialized cells. They are not only used in disease modeling and drug discovery but also in the creation of personalised regenerative therapies and future autologous transplantation approaches. Parallel to this, umbilical cord blood is currently being considered as an enriching regenerative source due to the presence of plentiful stem cells, immunomodulatory properties and other possible uses beyond traditional hematopoietic transplantation. Its continued use in the research to assess its role in tissue regeneration and immune-mediated disorders is continuing to support its increasing relevance in regenerative medicine (Allan, 2020).

7.3 Ex Vivo Stem Cell Expansion Technologies

The problem of limited dose of stem cells is also relevant especially in umbilical cord blood transplantation. Ex vivo stem cell expansion technologies aim to address this shortcoming by multiplying the amount of functional HSCs in pre-transplantation and maintaining their regenerative ability. The developments in culture systems, combinations of cytokines, small-molecule modulators, and bioreactor technologies have enhanced stem cell proliferation, increased the efficiency of engraftment, and speeded up hematopoietic recovery. It is hoped that such advances will make cord blood transplantation more applicable to adult patients, decrease graft failure and delayed immune reconstitution. The therapeutic potential of cord blood-derived stem cell products is also being enhanced by ongoing enhancement of expansion strategies (Gupta & Wagner, 2020).

7.4 Stem Cell Engineering and Cell-Based Drug Delivery

Stem cell engineering has gone beyond traditional transplantation to the creation of multifunctional cellular platforms that can deliver therapeutic delivery that is targeted. It is now possible to modify engineered stem cells to express therapeutic genes, to deliver anticancer genes, or to migrate selectively to tumor microenvironments, improving specificity of the treatment with reduced systemic toxicity. Such innovations have triggered a lot of interest in the field of hematological oncology, whereby stem cell-based drug delivery systems could enhance treatment effects of refractory or relapsing cancer. The combination of cellular engineering with biomaterials, nanotechnology, and molecular targeting therapies is still growing, broadening the clinical uses of stem cell-based therapeutics (Zhang et al., 2025).

7.5 Artificial Intelligence and Precision SCT

The impact of artificial intelligence (AI) on regenerative medicine is gradually becoming greater due to its ability to enhance the process of clinical decision-making across the entire pathway of SCT. Machine learning algorithms assist in the donor-recipient matching, prediction of transplantation risk, assessment of the quality of the graft, treatment planning, and post-transplantation monitoring by analyzing the clinical data. Artificial intelligence also helps in the discovery of biomarkers, prediction of transplantation outcome, and optimization of the personalized treatment strategy, which provides more informed clinical decisions. The combination of computational intelligence with regenerative medicine is thus anticipated to make the therapy more precise and efficient (Mukherjee et al., 2021).

7.6 Next-Generation Cellular Therapies

The new wave of stem cell-based therapies combines new methods of transplantations and novel cell products that are expected to enhance the effectiveness, availability, and clinical results. Cord blood has been regarded as an underexploited source for allogeneic transplantations and cell therapy owing to its distinctive biological nature and potential for new applications other than hematopoietic restoration (Shi et al., 2022). At the same time, the development of national transplant networks, alternative donors, and cellular therapies has provided the necessary clinical foundation for implementing next-generation stem cell treatments. Overall, all the developments discussed above contribute to the adoption of personalized, efficient, and available regenerative approaches for treating hematologic diseases (Xu et al., 2021). Table 3 presents the main developing technologies that will shape the future of SCT and regenerative hematology.

Table 3. Emerging Technologies Driving the Next Generation of SCT

Technology	Primary Purpose	Potential Clinical Application	Development Stage	Key References
Gene editing	Mutation correction	Hemoglobinopathies	Clinical translation	Kim et al., 2022
iPSC technology	Patient-specific cells	Regenerative hematology	Early clinical	Allan, 2020
Ex vivo expansion	Increase stem cell dose	Cord blood transplantation	Advanced clinical	Gupta & Wagner, 2020
Stem cell engineering	Targeted therapy	Drug delivery	Translational	Zhang et al., 2025
Artificial intelligence	Clinical decision support	Donor matching & prediction	Emerging	Mukherjee et al., 2021
Next-generation cellular therapies	Personalized therapy	Precision hematology	Rapidly evolving	Shi et al., 2022; Xu et al., 2021

8. Challenges, Ethical Considerations, and Future Directions

Although there has been a tremendous improvement in SCT, there are still numerous challenges that hinder its extensive use in clinical practice. Safety is a critical issue in the long-term perspective as recipients can develop graft failure, relapse of the disease, secondary malignancies, organ toxicity, and other late effects, and therefore the need to have long-term clinical follow-ups. Graft-versus-host disease and impaired immune reconstitution are still significant contributors to post-transplant morbidity and mortality, especially after allogeneic transplantation, and it is essential to develop better immune modulation and supportive care techniques.

The swift advancement of the stem cell technologies has also posed significant ethical and regulatory issues. Informed consent, privacy of donors, fair use of cord blood banking resources, commercialization of cord blood banking, and responsible utilization of gene-editing technologies are all problems that need strong regulatory and harmony of clinical standards across the borders. Moreover, the prohibitive prices of transplantation, lack of sufficient donor supply, and insufficient healthcare facilities still limit access to advanced stem cell treatments in most low- and middle-income nations, establishing major global differences in access to treatment.

Research in the future ought to be aimed at making transplantations safer, decrease the occurrence of immune-related complications, increase the amount of donors as well as coming up with more effective personalized treatments. New technologies such as gene editing, induced pluripotent stem cells, ex vivo stem cell expansion, artificial intelligence, and stem cell engineering are poised to continue to revolutionize regenerative hematology. To confirm these innovations and enable their safe implementation into regular clinical practice, extensive, multicenter clinical studies with follow-up will be necessary to ultimately enhance patient outcomes and increase access to stem cell-based therapies worldwide.

9. CONCLUSION

The application of SCT has radically changed the treatment of blood diseases by offering a regenerative and possibly curative treatment alternative to the traditional supportive and pharmacological methods. This is because this review has identified the central role of HSCs in the restoration of normal hematopoiesis and how the safety and accessibility of

HSCT has been enhanced by the progresses in blood banking, stem cell collection, processing, cryopreservation, and donor selection. The presence of several stem cells sources such as bone marrow, peripheral blood, umbilical cord blood, and induced pluripotent stem cells has enhanced therapeutic potential in a wide range of hematological disorders. The review also indicates that HSCT still forms the foundation of treatment of many non-malignant blood disorders, such as sickle cell disease, thalassemia, aplastic anemia, and primary immunodeficiency disorders, and is still an important curative approach to high-risk hematological malignancies, including leukemia, lymphoma, multiple myeloma, and myelodysplastic syndromes. The current advances in the field of gene editing, ex vivo stem cell expansion, stem cell engineering, artificial intelligence, and precision regenerative medicine are driving the shift towards more customized, effective, and safer methods of treatment. Regardless of these developments, long-term safety concerns, immune complications, ethical governance, availability of donors, costs of treatment, and global inequities continue to be significant obstacles to wider clinical use. Additional multidisciplinary efforts, technological progress, international cooperation, and equal access to advanced treatments along with the full potential of next-generation stem cell treatments to enhance the long-term prognosis and quality of life of blood disease patients will be needed.

REFERENCES

1. Mayani, H., Wagner, J. E., & Broxmeyer, H. E. (2020). Cord blood research, banking, and transplantation: achievements, challenges, and perspectives. Bone marrow transplantation, 55(1), 48-61.
2. Kurtzberg, J. (2017). A history of cord blood banking and transplantation. Stem cells translational medicine, 6(5), 1309-1311.
3. Shearer, W. T., Lubin, B. H., Cairo, M. S., Notarangelo, L. D., Section on Hematology/Oncology, Section on Allergy and Immunology, ... & Wang, J. (2017). Cord blood banking for potential future transplantation. Pediatrics, 140(5), e20172695.
4. Devi, S., Bongale, A. M., Tefera, M. A., Dixit, P., & Bhanap, P. (2023). Fresh umbilical cord blood—a source of multipotent stem cells, collection, banking, cryopreservation, and ethical concerns. Life, 13(9), 1794.
5. Dessels, C., Alessandrini, M., & Pepper, M. S. (2018). Factors influencing the umbilical cord blood stem cell industry: an evolving treatment landscape. Stem cells translational medicine, 7(9), 643-650.
6. Rao, I., Crisafulli, L., Paulis, M., & Ficara, F. (2022). Hematopoietic cells from pluripotent stem cells: hope and promise for the treatment of inherited blood disorders. Cells, 11(3), 557.
7. Querol, S., Rubinstein, P., & Madrigal, A. (2021). The wider perspective: cord blood banks and their future prospects. British Journal of Haematology, 195(4), 507-517.
8. Shi, P. A., Luchsinger, L. L., Greally, J. M., & Delaney, C. S. (2022). Umbilical cord blood: an undervalued and underutilized resource in allogeneic hematopoietic stem cell transplant and novel cell therapy applications. Current opinion in hematology, 29(6), 317-326.
9. Abusalah, M. A. H., Abd Rahman, E. N. S. E., & Choudhary, O. P. (2024). Evolving trends in SCT: an emerging and promising approach against various diseases. International journal of surgery, 110(11), 6862-6868.
10. Okeke, C., Silas, U., Okeke, C., & Chikwendu, C. (2021). Current trends on hemopoietic stem cells. Current Stem Cell Research & Therapy, 16(2), 199-208.
11. Chang, Y. J., Pei, X. Y., & Huang, X. J. (2022). Haematopoietic stem-cell transplantation in China in the era of targeted therapies: current advances, challenges, and future directions. The Lancet Haematology, 9(12), e919-e929.
12. Berglund, S., Magalhaes, I., Gaballa, A., Vanherberghen, B., & Uhlin, M. (2017). Advances in umbilical cord blood cell therapy: the present and the future. Expert Opinion on Biological Therapy, 17(6), 691-699.
13. Focosi, D., & Pistello, M. (2016). Effect of induced pluripotent stem cell technology in blood banking. Stem Cells Translational Medicine, 5(3), 269-274.
14. Zhang, P., Lin, R., Gao, J., & Ouyang, G. (2025). From stem cell transplantation to stem cell-based drug delivery systems targeting hematological malignancies: recent advances and clinical considerations. Expert Opinion on Drug Delivery, 22(11), 1751-1768.
15. Rahimi Darehbagh, R., & Rezaei, N. (2024). Introduction to SCT and Blood Cancers. In Hematological Cancer Diagnosis and Treatment: An Interdisciplinary Approach (pp. 1-15). Cham: Springer Nature Switzerland.
16. Passweg, J. R., Baldomero, H., Chabannon, C., Basak, G. W., de La Cámara, R., Corbacioglu, S., ... & European Society for Blood and Marrow Transplantation (EBMT). (2021). Hematopoietic cell transplantation and cellular therapy survey of the EBMT: monitoring of activities and trends over 30 years. Bone marrow transplantation, 56(7), 1651-1664.
17. Kiene, S., Albrecht, M., Theurich, S., Scheid, C., Skoetz, N., & Holtick, U. (2024). Bone marrow versus peripheral blood allogeneic haematopoietic stem cell transplantation for haematological malignancies in adults. Cochrane database of systematic reviews, (11).
18. Narayanan, D. L., & Phadke, S. R. (2019). Concepts, utility and limitations of cord blood banking: What clinicians need to know. The Indian Journal of Pediatrics, 86(1), 44-48.
19. Aly, R. M. (2020). Current state of stem cell-based therapies: an overview. Stem cell investigation, 7, 8.
20. Passweg, J. R., Baldomero, H., Bader, P., Bonini, C., Cesaro, S., Dreger, P., ... & Mohty, M. (2016). Hematopoietic stem cell transplantation in Europe 2014: more than 40 000 transplants annually. Bone marrow transplantation, 51(6), 786-792.
21. Juric, M. K., Ghimire, S., Ogonek, J., Weissinger, E. M., Holler, E., Van Rood, J. J., ... & Greinix, H. T. (2016). Milestones of hematopoietic stem cell transplantation–from first human studies to current developments. Frontiers in immunology, 7, 470.

22. Mallet, V., van Bömmel, F., Doerig, C., Pischke, S., Hermine, O., Locasciulli, A., ... & Ljungman, P. (2016). Management of viral hepatitis in patients with haematological malignancy and in patients undergoing haemopoietic stem cell transplantation: recommendations of the 5th European Conference on Infections in Leukaemia (ECIL-5). The Lancet infectious diseases, 16(5), 606-617.
23. Khandelwal, P., Millard, H. R., Thiel, E., Abdel-Azim, H., Abraham, A. A., Auletta, J. J., ... & Mehta, P. A. (2017). Hematopoietic stem cell transplantation activity in pediatric cancer between 2008 and 2014 in the United States: a center for international blood and marrow transplant research report. Biology of Blood and Marrow Transplantation, 23(8), 1342-1349.
24. Zhang, X. H., Chen, J., Han, M. Z., Huang, H., Jiang, E. L., Jiang, M., ... & Huang, X. J. (2021). The consensus from The Chinese Society of Hematology on indications, conditioning regimens and donor selection for allogeneic hematopoietic stem cell transplantation: 2021 update. Journal of hematology & oncology, 14(1), 145.
25. Ljungman, P., de la Camara, R., Robin, C., Crocchiolo, R., Einsele, H., Hill, J. A., ... & Ward, K. N. (2019). Guidelines for the management of cytomegalovirus infection in patients with haematological malignancies and after stem cell transplantation from the 2017 European Conference on Infections in Leukaemia (ECIL 7). The Lancet infectious diseases, 19(8), e260-e272.
26. Apperley, J., Niederwieser, D., Huang, X. J., Nagler, A., Fuchs, E., Szer, J., & Kodera, Y. (2016). Haploidentical hematopoietic stem cell transplantation: a global overview comparing Asia, the European Union, and the United States. Biology of Blood and Marrow Transplantation, 22(1), 23-26.
27. Xu, L. P., Lu, P. H., Wu, D. P., Sun, Z. M., Liu, Q. F., Han, M. Z., ... & Chinese Blood and Marrow Transplantation Registry Group. (2021). Hematopoietic stem cell transplantation activity in China 2019: a report from the Chinese Blood and Marrow Transplantation Registry Group. Bone marrow transplantation, 56(12), 2940-2947.
28. Ballen, K. (2017). Umbilical cord blood transplantation: challenges and future directions. Stem cells translational medicine, 6(5), 1312-1315.
29. Kim, J. Y., Nam, Y., Rim, Y. A., & Ju, J. H. (2022). Review of the current trends in clinical trials involving induced pluripotent stem cells. Stem cell reviews and reports, 18(1), 142-154.
30. Passweg, J. R., Baldomero, H., Bader, P., Bonini, C., Duarte, R. F., Dufour, C., ... & Mohty, M. (2017). Use of haploidentical stem cell transplantation continues to increase: the 2015 European Society for Blood and Marrow Transplant activity survey report. Bone marrow transplantation, 52(6), 811-817.
31. Niederwieser, D., Baldomero, H., Szer, J., Gratwohl, M., Aljurf, M., Atsuta, Y., ... & Gratwohl, A. (2016). Hematopoietic stem cell transplantation activity worldwide in 2012 and a SWOT analysis of the Worldwide Network for Blood and Marrow Transplantation Group including the global survey. Bone marrow transplantation, 51(6), 778-785.
32. Iida, M., Kodera, Y., Dodds, A., Ho, A. Y. L., Nivison-Smith, I., Akter, M. R., ... & Registry Committee of the Asia-Pacific Blood and Marrow Transplantation Group (APBMT). (2019). Advances in hematopoietic stem cell transplantation in the Asia-Pacific region: the second report from APBMT 2005–2015. Bone marrow transplantation, 54(12), 1973-1986.
33. Niederwieser, D., Baldomero, H., Bazuaye, N., Bupp, C., Chaudhri, N., Corbacioglu, S., ... & Saber, W. (2021). One and a half million hematopoietic stem cell transplants: continuous and differential improvement in worldwide access with the use of non-identical family donors. haematologica, 107(5), 1045.
34. Coombs, C. C., Zehir, A., Devlin, S. M., Kishtagari, A., Syed, A., Jonsson, P., ... & Berger, M. F. (2017). Therapy-related clonal hematopoiesis in patients with non-hematologic cancers is common and associated with adverse clinical outcomes. Cell stem cell, 21(3), 374-382.
35. Pietras, E. M. (2017). Inflammation: a key regulator of hematopoietic stem cell fate in health and disease. Blood, The Journal of the American Society of Hematology, 130(15), 1693-1698.
36. Allan, D. S. (2020). Using umbilical cord blood for regenerative therapy: Proof or promise?. Stem Cells, 38(5), 590-595.
37. Ilic, D., & Ogilvie, C. (2022). Pluripotent stem cells in clinical setting—new developments and overview of current status. Stem Cells, 40(9), 791-801.
38. Gupta, A. O., & Wagner, J. E. (2020). Umbilical cord blood transplants: current status and evolving therapies. Frontiers in pediatrics, 8, 570282.
39. Bergeron, A., Mikulska, M., De Greef, J., Bondeelle, L., Franquet, T., Herrmann, J. L., ... & Chemaly, R. (2022). Mycobacterial infections in adults with haematological malignancies and haematopoietic stem cell transplants: guidelines from the 8th European Conference on Infections in Leukaemia. The Lancet Infectious Diseases, 22(12), e359-e369.
40. Worel, N., Aljurf, M., Anthias, C., Buser, A. S., Cody, M., Fechter, M., ... & Halter, J. P. (2022). Suitability of haematopoietic cell donors: updated consensus recommendations from the WBMT standing committee on donor issues. The Lancet Haematology, 9(8), e605-e614.
41. Saez, B., Walter, M. J., & Graubert, T. A. (2017). Splicing factor gene mutations in hematologic malignancies. Blood, The Journal of the American Society of Hematology, 129(10), 1260-1269.
42. Penack, O., Peczynski, C., Mohty, M., Yakoub-Agha, I., Styczynski, J., Montoto, S., ... & Basak, G. W. (2020). How much has allogeneic stem cell transplant–related mortality improved since the 1980s? A retrospective analysis from the EBMT. Blood Advances, 4(24), 6283-6290.
43. Armitage, S. (2016). Cord blood banking standards: autologous versus altruistic. Frontiers in Medicine, 2, 94.
44. de la Fuente, J., Gluckman, E., Makani, J., Telfer, P., Faulkner, L., Corbacioglu, S., ... & Yesilipek, A. (2020). The role of haematopoietic stem cell transplantation for sickle cell disease in the era of targeted disease-modifying therapies and gene editing. The Lancet Haematology, 7(12), e902-e911.

45. Estcourt, L. J., Malouf, R., Trivella, M., Fergusson, D. A., Hopewell, S., & Murphy, M. F. (2017). Restrictive versus liberal red blood cell transfusion strategies for people with haematological malignancies treated with intensive chemotherapy or radiotherapy, or both, with or without haematopoietic stem cell support. Cochrane Database of Systematic Reviews, (1).
46. Cohen, S., Roy, J., Lachance, S., Delisle, J. S., Marinier, A., Busque, L., ... & Sauvageau, G. (2020). Hematopoietic stem cell transplantation using single UM171-expanded cord blood: a single-arm, phase 1–2 safety and feasibility study. The Lancet Haematology, 7(2), e134-e145.
47. Parikh, S., Brochstein, J. A., Galamidi, E., Schwarzbach, A., & Kurtzberg, J. (2021). Allogeneic stem cell transplantation with omidubicel in sickle cell disease. Blood advances, 5(3), 843-852.
48. Gibson, C. J., Kennedy, J. A., Nikiforow, S., Kuo, F. C., Alyea, E. P., Ho, V., ... & Lindsley, R. C. (2017). Donor-engrafted CHIP is common among stem cell transplant recipients with unexplained cytopenias. Blood, The Journal of the American Society of Hematology, 130(1), 91-94.
49. Pandey, D., Kaur, S., & Kamath, A. (2016). Banking umbilical cord blood (UCB) stem cells: awareness, attitude and expectations of potential donors from one of the largest potential repository (India). PloS one, 11(5), e0155782.
50. Mukherjee, S., Yadav, G., & Kumar, R. (2021). Recent trends in stem cell-based therapies and applications of artificial intelligence in regenerative medicine. World journal of stem cells, 13(6), 521.
51. Aljurf, M., Weisdorf, D., Alfraih, F., Szer, J., Müller, C., Confer, D., ... & El Fakih, R. (2019). Worldwide Network for Blood & Marrow Transplantation (WBMT) special article, challenges facing emerging alternate donor registries. Bone marrow transplantation, 54(8), 1179-1188.
52. Colom Díaz, P. A., Mistry, J. J., & Trowbridge, J. J. (2023). Hematopoietic stem cell aging and leukemia transformation. Blood, 142(6), 533-542.
53. Imran, S. A., M. Hamizul, M. H. A., Khairul Bariah, A. A. N., Wan Kamarul Zaman, W. S., & Nordin, F. (2022). Regenerative medicine therapy in Malaysia: an update. Frontiers in Bioengineering and Biotechnology, 10, 789644.

Recommended Figures

- **Figure 1.** Stem Cell Sources and Their Applications in Hematological Disorders
- **Figure 2.** Workflow of Blood Banking, Stem Cell Processing, and Cryopreservation
- **Figure 3.** Hematopoietic Stem Cell Transplantation Pathway from Donor Selection to Engraftment
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- **Table 1.** Comparison of Major Stem Cell Sources Used in Hematology
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